CANCER IN ONTARIO 1989

Community Cancer Control Networks

The Ontario Cancer Treatment
and Research Foundation

91-00407/

The Ontario Cancer Treatment and Research Foundation was incorporated in 1943 by an Act of the Legislature of the Province of Ontario and reconstituted by The Cancer Act, 1957. The Cancer Act states that, "The object of the Foundation is to establish and conduct a program of research, diagnosis and treatment in cancer, including,

(a) the establishment, maintenance and operation of research, diagnostic and treatment centres in general hospitals or elsewhere;

(b) the transportation of patients and escorts to its treatment centres or to the hospital of the Institute for diagnosis, treatment or investigation;

(c) the establishment, maintenance and operation of hostels in connection with its treatment centres or the hospital of the Institute;

(d) the laboratory and clinical investigation of cancer problems;

(e) the co-ordination of facilities for treatment;

(f) the adequate reporting of cases and the recording and compilation of data;

(g) the education of the public in the importance of early recognition and treatment;

(h) the providing of facilities for undergraduate and postgraduate study;

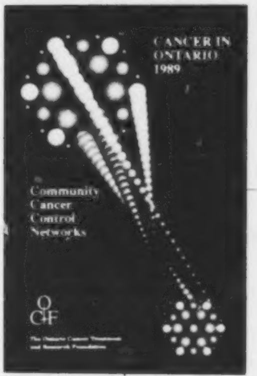
(i) the training of technical personnel; and

(j) the providing and awarding of research fellowships."

Part II of The Cancer Act, dealing with The Ontario Cancer Institute, as amended by The Cancer Amendment Act, 1968-69, provides that the Institute Board shall consist of 15 persons appointed by the Lieutenant Governor in Council. Five members of the Institute Board shall be representatives of the Foundation, one of whom shall be the chairman of the Foundation. The Act specifies that one of the Foundation representatives on the Board of the Institute shall be the chairman of the Institute.

Printed in Canada
ISSN 0315 - 9884

CANCER IN ONTARIO 1989


CANCER IN ONTARIO 1989
Community Cancer Control Networks
OCTF
The Ontario Cancer Treatment and Research Foundation

Community Cancer Control Networks

The Cover

This helix-like symbol represents the expansion of the OCTRF Regional Cancer Centres into the future (dark background). The precise configuration of the community cancer control networks concept and other future provincial programs is unknown but they will interact with other units of variable size to further extend the province's health care facilities into the community. The energy for this expansion will need to be highly focussed (columns of spheres in the centre foreground). The action unfolds against a background of variegated grey spheres representing: (i) the dynamism of oncology and (ii) the immense number of variables in the multicausal cluster of diseases called cancer. In view of our reliance on technology, it is fitting that this striking cover was drawn by computer.

The Ontario Cancer Treatment and Research Foundation
7 Overlea Boulevard
Toronto, Ontario, Canada
M4H 1A8

CONTENTS

Message from the Chairman 1

President's Report 3

James Harold Broughton 1910-1989 5

COMMUNITY CANCER CONTROL NETWORKS: A SYMPOSIUM

The Delivery of Cancer Care in Ontario in the 1990s 11

Cancer Incidence Projections for Ontario to the Year 2000 14

Long-Range Planning for Capital Needs 25

The Evolution and Development of a Community Cancer Clinic Network in the Province of Ontario 29

Summary of Education 33

REGIONAL CANCER CENTRES

OCTRF Regional Cancer Centres 37
- Hamilton Centre 39
- Kingston Centre 43
- London Centre 46
- Northeastern Ontario Oncology Program 49
- Ottawa Centre 51
- Thunder Bay Centre 58
- Toronto-Bayview Centre 61
- Windsor Centre 64

Service Load 67

Consultative and Follow-up Clinics by Zones of Service 73

Clinical Consultants at OCTRF Regional Cancer Centres and the Princess Margaret Hospital 75

THE ONTARIO CANCER INSTITUTE

The Ontario Cancer Institute incorporating the Princess Margaret Hospital 83

SPECIAL SERVICES

Provision of Drugs to Treat Malignant Disease 93

Carcinoembryonic Antigen (CEA) and Steroid-Receptor Assays 94

Diagnostic Biopsy Service and Voluntary Reporting by Pathologists 96

Lodges for Ambulatory Cancer Patients 96

Transportation of Cancer Patients 97

Cancer Information Service 97

Ontario Breast Screening Program 98

RESEARCH PROGRAMS

Summary of OCTRF Research 103

Research Personnel Supported by the OCTRF 106

Reports on Research Projects by City, Institution, Title and Author 107

EPIDEMIOLOGY AND STATISTICS

Errors in Cancer in Ontario 1988 184

Division of Epidemiology and Statistics 185

Cancer Incidence, Mortality and Treatment in Ontario 188

DIRECTORY

Members of the Ontario Cancer Treatment and Research Foundation and its Committees 209

Foundation Head Office Staff 214

APPENDICES

Appendix A: Bequests and Donations 217

Appendix B: List of Articles Published in 1988 by Research Personnel, Members of the OCTRF Staffs at the Regional Cancer Centres and Head Office and the staff of the OCI/PMH 223

MESSAGE FROM THE CHAIRMAN

Photo: Tony V. Hauser

In many respects 1989 was a watershed year for the Foundation. Having agreed to merge with the Ontario Cancer Institute/Princess Margaret Hospital (OCI/PMH) to form the Ontario Cancer Control Agency, we have been working with them and the Ministry of Health to develop a draft of a new Cancer Act. Our mission statement reads as follows:

> "The mission of the Ontario Cancer Treatment and Research Foundation, through its Regional Cancer Centres and in association with other institutions and agencies, is to decrease the incidence of and morbidity and mortality from cancer in Ontario through a co-ordinated, province-wide, cancer-control program including prevention, early detection, patient care, research, education and evaluation."

During the year an operational review, which the Foundation had initiated, was successfully completed. As a result, we have instituted a number of significant changes, including a reorganization of our management structure and the definition of our operating and capital needs.

Because of the continual growth in patient referrals during the year, pressures for delivering timely and appropriate radiotherapy in central Ontario (Toronto and Hamilton) reached a point where, with the co-operation of the OCI/PMH and the Canadian Cancer Society Ontario Division, mechanisms were developed to refer patients to other treatment centres, principally in Ontario. With the support of the Ministry, we are now recruiting and training additional personnel to extend operating hours even further and to plan new radiotherapy machine capacity to cope with projected needs in the 1990s.

A milestone in the development of new provincial initiatives of the Foundation was reached with the approval by the Ministry of Health of a breast screening program designed to screen women over 50 years of age every two years. This program was highlighted in Cancer in Ontario 1988.

We view as a positive initiative the appointment of a cancer co-ordinator for the Province as part of the Ministry's matrix management development.

As an indication of the support of the Foundation by Government, I wish to record a number of announcements regarding capital projects. On September 14, 1989 the Premier, the Hon. David Peterson, presided at a sod turning ceremony to initiate the construction of a new and expanded Hamilton Regional Cancer Centre. I had the pleasure during the year of accompanying the Minister, the Hon. Elinor Caplan, to Kingston, Ottawa and Sudbury for announcements on enhancements to our facilities in those regions. The visit to Sudbury was also marked by an announcement of funding by the Hon. Rene Fontaine, Minister of Northern Development, to promote a co-operative research program between our Northeastern Ontario Oncology Program and Laurentian University. Also, Mrs. Caplan has announced capital enhancement in Thunder Bay and Windsor. Finally, a mini-expansion of the Toronto-Bayview Regional Cancer Centre has been completed and the construction of a research facility with Sunnybrook Medical Centre and the University of Toronto progresses favourably.

A number of changes in Members of the Board are recorded with gratitude for their contributions to the governance of the Foundation. The appointments of Dr. L. Siminovitch, Dr. B.M. Thall and Mr. C. Waxman have been renewed. Ms. Laura Sabourin resigned. Dr. G.R. Walker's second term ended. The terms of Mr. A. Adams, Mr. G.P. Eligh, Dr. G.D. Hurteau, Mr. J.J. Kime, Mr. W. Livingston have expired and are under review. Mr. R.J. Potter has been replaced by Mr. M. MacKenzie by virtue of holding the office of the President of the Canadian Cancer Society Ontario Division.

The Ontario Cancer Care Fund, a joint undertaking with the OCI/PMH and the Canadian Cancer Society Ontario Division to raise $50 million for capital projects, continues under the leadership of the Hon. William Davis and Mr. John Mabley.

In closing, may I once again thank, through their Government, the people of Ontario, the Canadian Cancer Society Ontario Division, the staff of the Regional Cancer Centres and Head Office, OCI/PMH, host hospitals and medical schools for their continued support, which has made our programs of patient care, research and education meaningful realities.

Michael A. Meighen, Q.C.
Chairman

PRESIDENT'S REPORT

1989 was a year of challenges and change, a time of both satisfactions and tensions but also, I believe, a period of progress.

An Implementation Review Committee, composed of representatives from the Ministry of Health, Members of the Board and senior staff have addressed systematically the recommendations of the operations review, referred to by the Chairman. The Committee has been particularly active in organizational change, in the definition of operating and capital funding, information systems, communication with the Ministry and others, definition of Regional Cancer Centres and the drafting of a new Cancer Act to establish the Ontario Cancer Control Agency. The Committee hopes to complete its work in 1990.

The principal organizational changes have been the identification of an Executive Vice-President, who reports to the President, and the establishment of a Senior Management Committee made up of the Chief Executive Officers of the Regional Cancer Centres (now also Vice-Presidents of OCTRF) and senior Head Office staff.

Also we have established a Joint Liaison Committee with the Ontario Cancer Institute (OCI) and the Canadian Cancer Society Ontario Division to address issues of mutual concern.

People are the heart of any organization and must be regarded as a special resource. We are working with the OCI and the Ministry on workload standards. Our Human Resources Department has been active in the development of policies and procedures, labor relations, compensation and benefits, planning for pay equity, management training and the implementation of the French Language Act.

It is a pleasure to record that the Toronto-Bayview Regional Cancer Centre has received its second accreditation from the Canadian Council of Health Facilities Accreditation for a period of three years.

I cannot comment on all staff changes but I wish to recognize several. Mr. R.D. Gray, former Secretary-Treasurer and chief administrative officer of the Foundation, retired in August after many years of faithful service. Mr. A.R. Ganderton, who became our interim Chief Operating Officer (COO) in July, has done an outstanding job. In 1990, Mr. Harold Wodinsky, the COO of the Toronto-Bayview Regional Cancer Centre will assume the role of the COO of OCTRF. Dr. E.A. Clarke, Head of the Division of Epidemiology and Statistics and Vice-President of OCTRF, has become the Cancer Co-ordinator for the Ministry of Health on a part-time basis. Mr. Nelson Devereaux has joined us as Chief Financial Officer.

During the year we were saddened by the death of Mr. Harold Broughton, the original Secretary-Treasurer who served the Foundation from 1946 to 1977.

On the national front I am a member of a national task force, Cancer 2000, to examine strategies for cancer control in Canada at the national, provincial and local levels. This work is funded by Health and Welfare Canada and the Canadian Cancer Society.

On the international level we are working with the Canadian Cancer Society and the National Cancer Institute of Canada to bring the UICC International Cancer Congress to Montreal in 1994.

Elsewhere in this issue, in a section devoted to cancer care in the 1990s, I have outlined our role in the past, the present and some of the strategic issues we must address in the future.

In closing I wish to thank the Board, the Regional Cancer Centres and the Head Office staff for their support in these challenging times. Finally I wish to acknowledge support of the work of the Foundation by the Government of Ontario, the Canadian Cancer Society Ontario Division and the many patients, their families and friends without whose help we could not complete our task.

J. William Meakin, M.D., F.R.C.P.(C)
President and Chief Executive Officer

No annual financial statement is included in *Cancer in Ontario* but a copy of such statement will be provided upon request to the Head Office of the Foundation.

James Harold Broughton
1910-1989

JAMES HAROLD BROUGHTON
1910–1989

With great sadness we share with our readers the passing of "Mister Foundation" - James Harold Broughton - on August 21, 1989, in Toronto.

Mr. Broughton was born in Toronto on April 15, 1910. He attended public school in Toronto proceeding to senior matriculation at the University of Toronto Schools in 1928. He attended the University of Toronto (Victoria College) and graduated with his B.Comm. in 1932. He earned his C.A. from the Institute of Chartered Accountants of Ontario in January 1936 while employed by Clarkson, Gordon, Dilworth and Nash. In June 1940, he joined the Royal Canadian Air Force and served for five years in the Accounts Branch, returning to civilian life in June 1945, with the rank of Squadron Leader.

Mr. Broughton was appointed to the post of Secretary-Treasurer of the OCTRF in June 1946 and he served in that capacity with diligence and distinction until June 30, 1977. He continued as secretary to June 30, 1978, and then as financial consultant until his retirement on December 30, 1978, after more than 32 years of service.

At the time of Mr. Broughton's retirement, the late Dr. W.G. Cosbie, a former medical director, noted "Harold Broughton's long service to the Ontario Cancer Foundation can hardly be summed up in words. With the growth of the institution, his financial expertise has been an unfailing sheet anchor. While other spent, he provided. He has been a perfect running mate for the medical directors, always aware of the problems they had to face and was an invaluable liaison with the Canadian Cancer Society."

The late Dr. A.H. Sellers, a colleague for many years, said "Harold Broughton's many talents fitted him for a vital role in the development of the Foundation - his incredible memory for detail, his integrity, his industry and dedication. He had an excellent working relationship with his staff, due in large measure to his sensitivity to individual needs and his good humor. From the time of my appointment as Consultant in Medical Statistics to the Foundation in 1948, Harold recognized the need for the development of a strong Foundation program in the field of epidemiology and statistics. He gave his full support toward this end and I thank him especially warmly for his wisdom in this area. Harold's duties and responsibilities were varied; he provided leadership and support in all areas of the Foundation's activity. From time to time he was, in effect, an executive director, an administrator, a planner and, for many years, the editor of the Foundation's *Annual Report*. There is no doubt that he has made, over three decades, a major contribution to the development and operation of the cancer control program in Ontario."

The late Dr. D.E. Cannell, another medical director, remembered: "The financial welfare of the Foundation was close to his heart. Its eminently satisfactory situation was due, in no small part, to his astute activities as guardian of its steadily increasing funds. At all times, within my memory, he was impelled to lead and aid all its manifold activities. Always before him was the goal of producing the greatest benefit in the diagnosis and management of cancer for the people of Ontario. Many of its medical personnel, research grantees, fellows and associates were unaware of the beneficial effects of his support in crucial decisions involving a variety of projects. Without his interest and activity, the broad services now supplied to cancer patients in Ontario would not be available."

Judge J.R.H. Kirkpatrick, former Chairman of the Board, remembers him: "Harold Broughton served as secretary to the Foundation Board and to most of the committees of the Foundation. Consequently, he assembled or prepared and presented much of the material that shaped the policy and programs of the Foundation. In his role as treasurer he showed exceptional skill in acquiring, investing and husbanding the funds of the Foundation. He performed the duties of unproclaimed personnel officer supervising an efficient staff and conscientiously presenting their views and interests to the Board. Because his knowledge, capabilities and experience extended far beyond the scope of his profession, he was able to play a major role in the planning, administration and execution of the programs of the Foundation. The best illustration of Harold's ability and personality is that during the 32 years he served as secretary and treasurer with six medical directors, each one a brilliant and dynamic individual, never was it deemed necessary to define his position and that of the medical director or delineate the scope, responsibilities and authorities of those offices. He worked effectively in partnership with these eminent physicians in the administration and operation of the programs of the Foundation."

Mr. Broughton is survived by his widow, Esther Margaret, three children - Catherine Margaret, M.D., Thora Kirstin, and Alan James, and four grandchildren - Adam, Alyssa, Erik and David. He will be greatly missed and fondly remembered by his family, friends and colleagues.

COMMUNITY CANCER CONTROL NETWORKS: A SYMPOSIUM

THE DELIVERY OF CANCER CARE IN ONTARIO IN THE 1990s

J.W. MEAKIN, M.D.*,
Toronto, Ontario

Origins

The Foundation had its origins in 1931 when the Province established a Royal Commission to inquire into the use of radium and x-rays for the treatment of the sick and to recommend a system of cancer treatment, research and education in Ontario. In 1932, the Commision reported to the Legislative Assembly and in 1943 the Cancer Act was passed establishing the Ontario Cancer Treatment and Research Foundation. In 1952 the Act was amended to establish the Ontario Cancer Institute incorporating the Princess Margaret Hospital and was amended again in 1972 to provide for the confidential collection of information on cancer patients.

The Present

Over the past 45 years, the Foundation has evolved into a effective cancer control agency, supported centrally by the Government but functionally rooted in the community. Our major responsibilities are a natural and interdependant triad, namely: provision of treatment for cancer; support of research in cancer; and the provision of education in cancer, directed to both the health profession and the lay public.

The heart of the Foundation is its eight regional cancer centres. These are located in Thunder Bay in the northwest, Sudbury in the northeast, Ottawa and Kingston in the east, London and Windsor in the southwest, and Hamilton and Toronto centrally. Each centre is attached to a host hospital to reduce costs in providing beds and diagnostic support service. The centres are staffed by full-time specialists in radiation and medical oncology supported by consultant specialists drawn from the community served. The centres provide two important elements in cost-effective cancer care, namely: the regionalization of expensive, high-technology radiotherapy equipment and the milieu for multidisciplinary decisions on the optimal method of managing the patient. On a regular basis, staff members from the centres travel to over 20 community hospitals throughout the Province to see new and old patients, to minimize travel for these patients and to maintain contact with community doctors. Whenever possible, patients, who come to the centres for treatment, are housed in lodges or hostels.

---

*President and Chief Executive Officer, The Ontario Cancer Treatment and Research Foundation, Toronto.

In addition to the regional cancer centres, the Foundation supports a number of Provincial programs some of which are carried out through the regional cancer centres.

The Foundation pays travel costs for needy patients, who come from more than 25 miles to the regional cancer centres. Also it provides anti-cancer drugs to needy patients anywhere in the Province where there is no other mechanism for cost recovery. Some cancer diagnostic tests are subsidized in selected regional laboratories using a closed-ended budgeting mechanism.

The Foundation supports training or educational experiences in cancer medicine for: medical students, physics students, radiation technologists, nurses, radiation oncologists, medical oncologists, research scientists and also provides continuing medical education for medical practitioners.

In the field of research, the Foundation supports basic and clinical research scientists in its centres and in the health sciences complexes of the Province. Further, we have inaugurated a program of clinical trials research (Ontario Clinical Oncology Group) centred in Hamilton but integrating research workers in its eight centres, the Ontario Cancer Institute incorporating the Princess Margaret Hospital and the five medical schools.

Education and research are essential if Ontario residents are to receive first-class treatment at the "cutting edge" of world knowledge. However, for forward planning of treatment, education and research, we need accurate knowledge concerning the dimensions of the cancer problem in Ontario at any given time; we need to know how this group of diseases is changing and need to determine whether our current treatment methods are optimal. Thus the Foundation operates the Ontario Cancer Registry, which compiles a record of all cancer cases by diagnosis, age, sex, residence and other appropriate factors.

Future — The 1990s

While we can be proud of the past, we must plan for the future. Planning whether for programs or capital facilities requires information on incidence, mortality and prevalence to define the dimension of the problem. In a subsequent article "Cancer Incidence Projections for Ontario to the Year 2000", Dr. J. McLaughlin and Mr. W. King describe how this vital information base is assembled.

Planning for capital requirements to deliver cancer care, our primary mandate, is discussed in a following article by Messrs. R. Ganderton and S. Gattesco.

Planning for new programs continues.

A breast screening program, which is about to be launched, was the focus of Cancer in Ontario 1988.

The Foundation is completing active plans for Community Cancer Clinic Network, which will link functionally our regional cancer centres with the communities they serve. Dr. J. Gowing describes this challenging venture in the closing article of this section.

Other areas, which need to be addressed, include prevention, surgical oncology, psychosocial care, new education initiatives both professional and public, and a continuing refinement of our research programs and quality assurance.

We need to envision and plan for new services but this must be done in the context of fiscal reality. The Foundation, the Canadian Cancer Society Ontario Division and the Government face a constant challenge to find ways to fund capital and operating programs within a finite fiscal resource base while preserving a sense of priority and quality assurance.

The future success of cancer control in the 1990s is being advanced by organizational changes in which the Ontario Cancer Institute incorporating the Princess Margaret Hospital and the Ontario Cancer Treatment and Research Foundation will merge into the Ontario Cancer Control Agency under a new Cancer Act now being drafted. We believe the Agency will enhance the co-operative efforts of the Ontario Cancer Institute incorporating the Princess Margaret Hospital and the Ontario Cancer Treatment and Research Foundation and also those of the Canadian Cancer Society Ontario Division and other institutions that contribute to our progress in prevention, cure and care.

CANCER INCIDENCE PROJECTIONS FOR ONTARIO TO THE YEAR 2000

J. McLAUGHLIN, M.Sc.,Ph.D.*, W. KING, M.Sc.**,
Toronto, Ontario

The population of Ontario is growing and aging, a trend that is expected to continue for the next decade. The estimated population for Ontario in 1990 is 9.7 million and by the year 2000 it is projected to grow to 10.9 million, an increase of 12%. From 1990 to 2000, the median age is expected to rise from 33.6 to 37.9 years and the number in the population who are aged 65 or greater is expected to grow from 1.14 to 1.47 million, an increase of 26%[1]. These increases in population size and the proportion of older citizens will have a direct effect on the future cancer burden in Ontario.

This paper examines the expected cancer burden through the 1990s by means of projected estimates of the annual number of incident cancer cases, i.e., new cases of malignant cancer in the population. Such projections serve as an aid in planning services, which will be part of the provincial cancer control system during the next decade. We give the projected numbers of incident cancer cases for Ontario as a whole, for five regions of the province and for the most important specific types of cancer.

Methods

The Ontario Cancer Registry (OCR) supplied the number of incident cancer cases that have occurred in recent years in Ontario. The OCR is described elsewhere, in the report of the Division of Epidemiology and Statistics. Reports of "incidence" refer to new diagnoses of all malignant neoplasms, excluding non-melanotic skin cancer [International Classification of Disease (ICD) - Ninth Revision codes 140-208, excluding 173]. To predict the number of incident cancer cases for Ontario until the year 2000, we require two additional types of information: the expected incidence rates and the expected populations.

---

* Senior Epidemiologist, Division of Epidemiology and Statistics, Ontario Cancer Treatment and Research Foundation, Toronto.

** Biostatistician, Division of Epidemiology and Statistics, Ontario Cancer Treatment and Research Foundation, Toronto.

The expected incidence rates were obtained by extrapolating the recently observed trend in incidence rates in Ontario. Cancer incidence frequencies in Ontario for the years 1979 to 1987, subdivided by gender and four age groups (0-14, 15-44, 45-64 and 65+ years), were obtained from the OCR. Intercensal population estimates from Statistics Canada[2,3] were used to calculate incidence rates for each of the strata defined by gender and age groups. For each stratum, the logarithm of the incidence rate was regressed on time: these regression models were used to predict the incidence rate for any year in the near future.

The expected population for each sex, age group and county was obtained from the Ministry of Treasury and Economics[1]. The population projections used in this study were the most recent available, being based on the 1986 census and were for the "reference scenario", which assumes medium levels of fertility and migration.

The projected number of incident cancer cases was calculated for each sex and each year to 2000 by multiplying the projected Ontario incidence rates, stratified by age and sex, by the stratum-specific populations and then summing across the age strata. Projections were obtained first for "all sites of cancer combined" in Ontario.

A second set of projections was obtained for "all sites of cancer combined" in five planning regions of the province. The five regions, which are groupings of counties used for planning purposes by the Government of Ontario[4], include Southwestern, Central, Eastern, Northeastern and Northwestern Ontario. The counties included in each planning region are listed in an appendix. For each region, the projected number of incident cases was estimated by applying the projected incidence rates for Ontario to the projected populations of the region.

The third series of projections was for specific cancer sites for the whole province. Incidence frequencies were obtained from the OCR for the five leading sites of cancer for males and females separately. Incidence projections for Ontario were obtained in the same manner as described above for "all sites combined".

Results

Figure 1 shows the actual (1979-1987) and projected (1988-2000) numbers of incident cancer cases among males and females in Ontario. Table I provides the data, which are plotted in Fig. 1; in addition, it lists the total number of incident cases in both sexes. For the period 1979-1987, the actual number of incident cases increased from 27 960 to 36 501. From 1990 to 2000, the total number of incident cases is projected to rise from 40 982 to 58 729 - an average annual increase of 3.7%, whereas the average annual increases by sex were 3.9% for males and 3.4% for females.

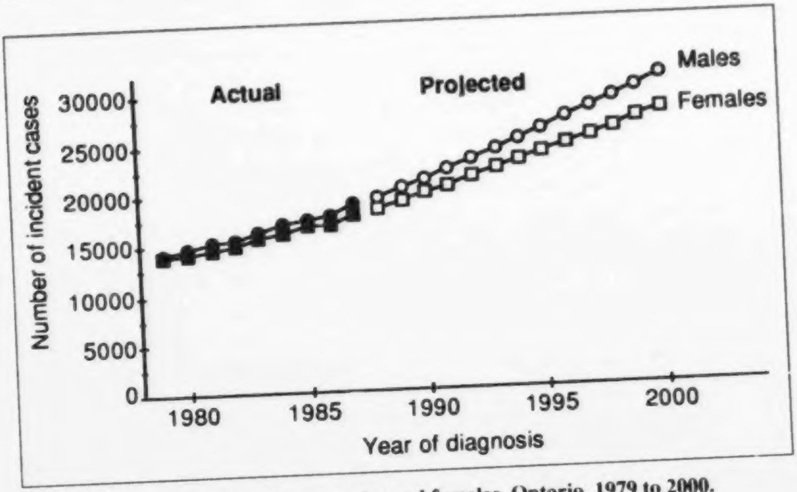


Fig. 1. Cancer incidence, males and females, Ontario, 1979 to 2000.

TABLE I

Actual Cancer Incidence, 1979 to 1987, and Projected Cancer Incidence 1988 to 2000, of Ontario

YEAR		ONTARIO INCIDENCE		ONTARIO INCIDENCE
		Males	Females	(both genders)
Actual	1979	14,138	13,822	27,960
	1980	14,668	14,125	28,793
	1981	15,206	14,488	29,694
	1982	15,486	14,774	30,260
	1983	16,238	15,679	31,917
	1984	16,876	16,060	32,936
	1985	17,341	16,746	34,087
	1986	17,714	16,741	34,455
	1987	18,823	17,678	36,501
Projected	1988	19,552	18,354	37,906
	1989	20,386	19,050	39,436
	1990	21,233	19,749	40,982
	1991	22,115	20,471	42,586
	1992	23,076	21,249	44,325
	1993	24,040	22,023	46,063
	1994	24,994	22,791	47,785
	1995	25,981	23,580	49,561
	1996	26,988	24,377	51,365
	1997	27,976	25,175	53,151
	1998	28,988	25,996	54,984
	1999	29,990	26,829	56,819
	2000	31,035	27,694	58,729

Table II lists the total number of projected incident cases for each of the five planning regions and for Ontario as a whole in the years 1990, 1995 and 2000. Table II also lists the projected populations upon which the incidence projections are based. We expect the largest number of cases in the Central region, which contains communities with large populations such as Metropolitan Toronto and the regional municipality of Hamilton-Wentworth. The Central region had the greatest proportionate increase in population between 1990 and 2000 (14%), resulting in the greatest proportionate increase in incidence (47%). By the year 2000, 38 228 cases are expected in the Central region, which is expected to have a population of 7.14 million.

In the Eastern region, incidence is expected to rise from 5791 to 8110 from 1990 to 2000, an increase of 40%. In Southwestern Ontario, the number of incident cases will be similar but the rate of change will be slightly lower in Southwestern Ontario, a 33% increase is expected from a level of 5949 in 1990. The Northeastern region will have 2342 cases in 1990 and 3129 in 2000 - a rise of 34%. Northwestern Ontario will have a similar increase, 35% from a 1990 level of 986 incident cases. From 1990 and 2000, we project the total growth in the populations of the Eastern, Southwestern and Northwestern regions to range between 5% and 10%. For the Northeastern region the population is projected to decrease slightly, by 1%.

Regarding Table II, we must emphasize that for each region the same projected incidence rates were employed, namely, the age and sex specific rates for Ontario. Crude incidence rates can be calculated for each region from the data in Table II by dividing the number of incident cases by the population. In the year 2000, the crude annual incidence rates will range from 5.22 per 1000 for the Northwestern region to 5.59 per 1000 for the Northeastern region. Since the incidence rates for each age-sex stratum are identical, the regional differences in the crude incidence rates are due to variation in the age and sex distributions of the projected populations. For example, the relatively high crude incidence rate in the Northeastern region is due to a large projected reduction in the number of young people, e.g., due to migration from the area; hence older citizens, fewer of whom will move away from the area, will constitute a larger proportion of the population.

TABLE II

Projected Cancer Incidence and Population According to Regions of Ontario, 1990 to 1995 and 2000.

REGION *	1990		1995		2000	
	Incidence	Population	Incidence	Population	Incidence	Population
Northwestern	986	245,397	1,156	251,921	1,339	256,360
Southwestern	5,949	1,340,491	6,901	1,391,584	7,923	1,438,002
Central	25,914	6,230,143	31,865	6,732,879	38,228	7,139,293
Eastern	5,791	1,364,864	6,909	1,445,764	8,110	1,502,699
Northeastern	2,342	567,843	2,729	564,382	3,129	559,442
Prov. of Ontario	40,982	9,748,737	49,561	10,386,529	58,729	10,895,996

*Refer to appendix for definition of regions.

Figure 2 shows the actual and projected incidence frequencies for five sites of cancer for men. The sites are those with the highest projected frequencies in 1990. In Fig. 2, the five sites for males are lung, bronchus and trachea (ICD-9 162; referred to in the figures and text as "lung cancer"), prostate (ICD-9 185), intestine and rectum (ICD-9 152-154), bladder (ICD-9 188) and the lymphomas (ICD-9 200-202).

The most remarkable feature of Fig. 2 is the large increase in the projected number of incident prostate cancer cases. In 1990 we project that prostate cancer will be the second most common cancer, accounting for 18% (3847/21 233) of all cancers in males: this is only slightly less than the proportion of lung cancers - 20% (4249/21 233). Prostate cancer is projected to surpass lung cancer by 1995 and to account for 22% of all male cancer in 2000. Whereas the average annual increase between 1990 and 2000 is 6.0% for prostate (from 3847 to 6907 cases), it is 3.4% for lung cancer (from 4249 to 5943).

Each of the five leading cancers in males will show a steady increase in the number of incident cases between 1990 and 2000. Although the differences in the number of cases are smaller for intestine-rectum cancer, bladder cancer and the lymphomas than for prostate or lung cancer, the proportionate changes are still substantial. For intestine-rectum cancer, bladder cancer and the lymphomas, the average annual increases will range between 3.3% (bladder) and 4.6% (lymphomas): these are similar to the increase for all sites of cancer combined (Fig. 1).

The five cancer sites in females are plotted in Fig. 3 and include breast (ICD-9 174), intestine-rectum (ICD-9 152-154), lung, bronchus and trachea (ICD-9 162), uterus (ICD-9 179, 181, 182) and the lymphomas (ICD-9 200-202). These incidence projections indicate that, on the basis of recent trends, breast is likely to remain the most common cancer among women during the next decade. Breast cancer is projected to account for 26% (5221/19 749) of all cancers among women in 1990 and 28% (7711/27 694) of all cancers in 2000. The number of breast cancer cases is expected to increase from 5221 in 1990 to 7711 in 2000 -a 4.0% average annual increase.

Lung cancer in women will show the most remarkable change in projected incidence. In 1990, lung cancer will account for 12% (2367/19 749) of all female cancers, whereas by 2000 it will account for 20% (5513/27 694). During this period, the annual number of female lung cancers will more than double (from 2367 in 1990 to 5513 in 2000) and will increase annually by an average of 8.8%. Intestine-rectum cancer, the second most frequent cancer among women in 1990, is expected to increase annually by 2.5%. Lung cancer is expected to replace intestine-rectum cancer as the second most common cancer in women by 1994.

The expected rise in the number of uterine cancers was quite small - an average annual increase of 1.5% from a 1990 level of 1101 cases. The number of female lymphomas will show a pattern of increase similar to that for males, with a 3.9% average annual increase between 1990 and 2000.

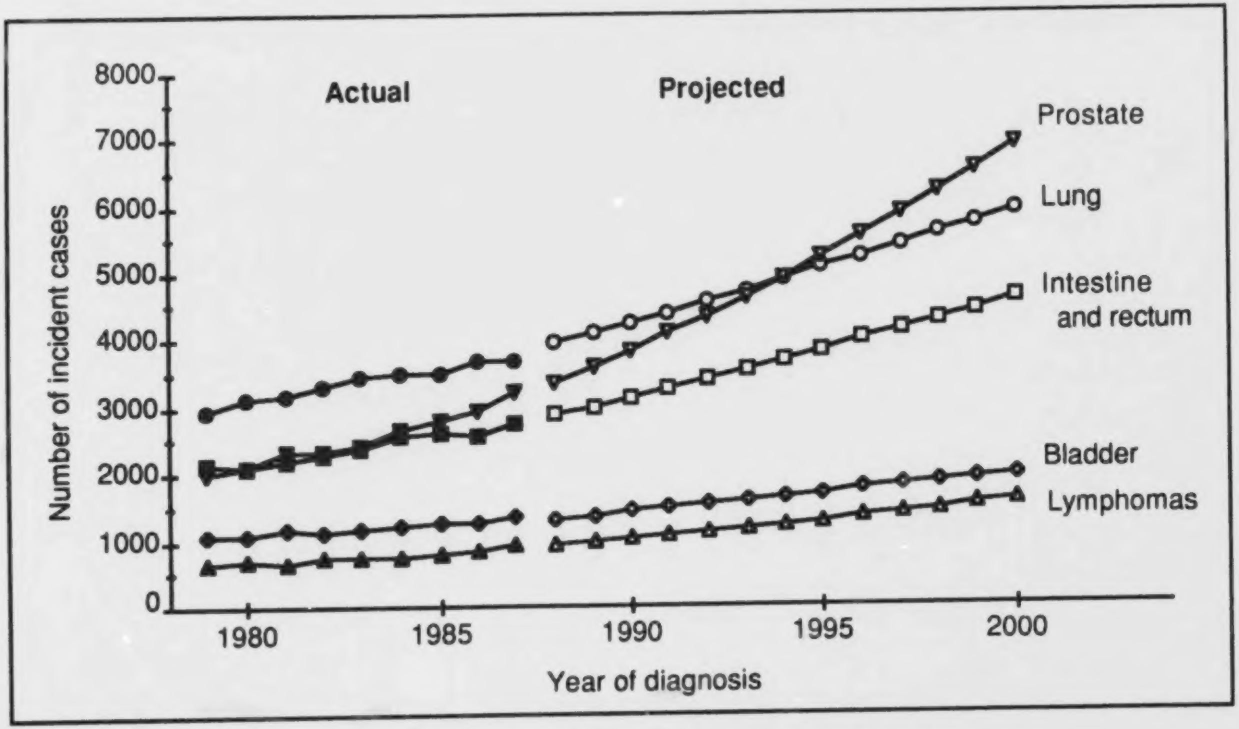


Fig. 2. Cancer incidence in males, selected sites, Ontario, 1979 to2000.

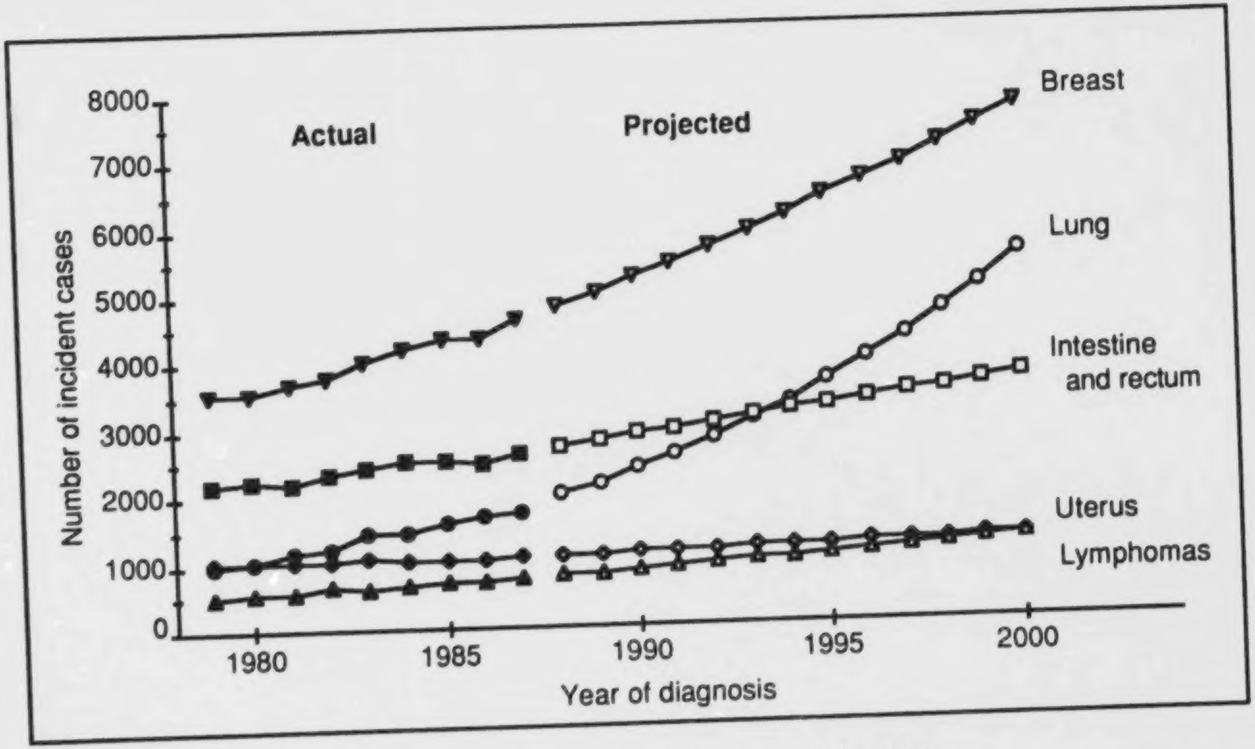


Fig. 3. Cancer incidence in females, selected sites, Ontario, 1979 to 2000.

Discussion

The number of incident cancer cases is projected to increase annually by 3.6% between 1990 and 2000 in Ontario. Similar increases in incidence were projected for both sexes and for each of the five planning regions of the province. These results have important implications for Ontario's cancer control services and indeed for the whole health-care delivery system.

Two factors will contribute to the dramatic increase in the number of incident cancer cases in Ontario in the 1990s: changes in the population structure, e.g., increases in size and proportion of older citizens, and increases in the age-specific cancer incidence rates. We tested the relative importance of these two factors by estimating the incidence in 2000 while fixing one factor at the 1990 level. The impact of a changing population was examined by obtaining estimates with the incidence rates fixed at the 1990 level while the population growth was allowed to follow the projected patterns. The impact of the changing incidence rates was determined by fixing the population at the 1990 level and allowing the incidence rate to change. This exercise demonstrated that the major contributor to the increase in cancer incidence in Ontario is change in the population structure rather than the projected increase in incidence rates. An important feature of the population change is the increasing proportion of older individuals among whom most of the new cancer cases develop.

The projections of incidence for the five most frequent cancer sites indicate the continuing importance of lung cancer. We project it will be the leading cause of cancer in males until 1995, at which time it will be surpassed by prostate cancer. In females, lung cancer will be the third most common cancer until 1993, at which time it will move into second place. The projected increase in female lung cancer incidence is dramatic and its annual increase was greater than at any other site.

In interpreting the lung-cancer projections, certain underlying assumptions must be considered. These projections are based on the observed age- and sex-specific incidence rates for Ontario from 1979 to 1987. It is valid to extrapolate these rates into the future assuming that there are no significant changes in exposure to the various causes of cancer. Therefore, when interpreting these projections, the potential for a change in the expected incidence rates due to risk factor modification must be examined.

It is widely accepted that a large proportion of lung-cancer cases can be attributed to cigarette smoking[5]. Lung-cancer rates have increased in parallel with, but 20 years after, increases in smoking rates over the past 50 years[6,7]. Thus, while recent trends in tobacco use, e.g., number of smokers, quantity smoked and use of low-tar cigarettes, have important implications for the future pattern of lung-cancer incidence, we may not be able to detect the impact on incidence for many years.

We can anticipate some changes in the projected rates and incidence of lung cancer in response to changes in observed smoking habits over the last 20 years. In males, during the period 1990 to 2000, lung-cancer incidence rates and frequencies are likely to be lower than projected because smoking prevalence has declined steadily between 1966 and 1986. In 1966, 50% of males in Ontario, aged 15 years and over, smoked regularly compared to 28% in 1986[8]. In females, however, the decline in smoking prevalence is much less pronounced. About 31% of Ontario women, aged 15 year and over, smoked regularly in 1966 compared to 24% in 1986[8]. Thus, the lung-cancer rates projected for females in the next decade are not likely to be greatly affected by the reductions in smoking that have been achieved to date.

We must interpret cautiously the projected increase in the number of incident prostate cancer cases. Prostate cancer, a common cancer in older men, is extremely rare in young males. Because of symptom-free and undetected tumors[9], the true incidence in older men may be greater than hitherto reported. In recent years the incidence rate of prostate cancer has been increasing worldwide[10]. The increasing rates can be attributed partially to advances during the 1970s that allowed the detection of less advanced disease[11]. It is possible that more effective detection has contributed to the large increase in the observed prostate cancer rates. If the number of early-staged cases continues to rise at the same rate as it has in recent years, e.g., if the methods of early detection are applied gradually throughout the province, it is possible that we may see the large increase in prostate cancer cases projected here. Otherwise, the large increase in rates from 1979 to 1987, i.e., the years on which these projections are based, would produce overestimates of the projected rates and, in turn, an overestimate of the projected incidence. Nevertheless, the implications of these projections are important: they indicate that prostate cancer will become increasingly common. Even though prostate cancer has a better prognosis than lung cancer, it will absorb major cancer-control resources in Ontario in the 1990s.

Incidence is only one of the many indicators of disease burden in a population. Elsewhere this volume gives the 1987 estimates of incidence rates and mortality rates (see the report of the Division of Epidemiology and Statistics). In the short-term, projections of incidence are reliable as long as there is a continuation of recent trends in population growth and incidence rates. Incidence frequencies, which describe the total number of new cases, are particularly valuable as indicators of the future challenges to the cancer control system.

The projections of incidence for Ontario indicate that each component of the cancer-control system will face new challenges in the 1990s. There are important implications for diagnostic and treatment services in Ontario since all cases detected will require such services. The analysis by region indicates that every region of the province can expect an increase in cancer incidence. Due to the variations in population, the challenges to be faced in each region will vary. For example, in the heavily populated Central region, the major challenge will be to provide service to the large and rapidly increasing number of cancer cases expected over the next decade. The Northeastern and Northwestern regions face a slightly different and continuing challenge, namely, to provide services to cancer patients spread over an enormous geographical area. The analysis by cancer site indicates the relative frequency of the five most common sites and therefore points to where treatment advances will have the greatest impact.

One of the major challenges for the cancer-control system is to reduce cancer incidence rates. This will require the further development and implementation of screening programs that allow the detection of precursor (precancerous) lesions. Screening programs that enable the early detection of cancer, e.g., breast, may result in an even higher site-specific incidence than has been projected here. For some sites of cancer it is therefore conceivable that, in order to achieve long-term reductions in late-stage disease and mortality, there may need to be an increase in the detection of early-stage disease. Another important preventive strategy is to reduce the exposure to known causes of cancer. Increased efforts in the 1990s to reduce tobacco use may lead to declines in lung-cancer rates in the long-term but such an effect is unlikely during this decade. In the short-term, therefore, treatment will be required for these large number of lung cancer cases.

A comprehensive approach to the control of cancer in Ontario is required. During the next decade, cancer-control agencies will be challenged to provide quality diagnostic and treatment services to an increasing number of cancer patients. An additional goal must be the development of prevention and screening strategies that further reduce long-term morbidity and mortality.

ACKNOWLEDGEMENTS

We gratefully acknowledge the assistance of Peter Toogood in computer programming and Jean Rowan in the preparation of the manuscript.

REFERENCES

1. Demographic Bulletin: Population Projections for Regional Municipalities, Counties and Districts of Ontario to 2011. Toronto: Ontario Ministry of Treasury and Economics, 1989.
2. Revised Annual Estimates of Population, by Sex and Age Group, Canada and the Provinces. Ottawa: Statistics Canada, 1981.
3. Revised Annual Estimates of Population, by Sex and Age Group, Canada and the Provinces. Ottawa: Statistics Canada, 1986.
4. Ontario Statistics - 1982. Toronto: Ontario Ministry of Treasury and Economics, 1983.
5. Hammond EC, Seidman H: Smoking in the United States. *Prev Med* 1980; **9**: 169.
6. Kristein MM: Forty years of U.S. cigarette smoking and heart disease and cancer mortality rates. *J Chron Dis* 1984; **37**: 317.
7. Fraumeni JF, Blot WJ: Lung and Pleura. *In*: Schottenfeld D, Fraumeni JF, eds. Cancer Epidemiology and Prevention. Philadelphia: W.B. Saunders, 1982: 564.
8. Health and Welfare Canada. The Smoking Behaviour of Canadians 1986; by W.J. Millar. Ottawa: Minister of Supply and Services Canada, 1988.

9. Wynder EL, Mabuchi K, Whitmore WF: Epidemiology of cancer of the prostate. *Cancer* 1971; **28**: 344.
10. Parkin DM, Laara E, Muira CS: Estimates of the worldwide frequency of sixteen major cancers in 1980. *Int J Cancer* 1988; **41**: 184.
11. Murphy GP, Natarajan N, Pontes JE et al: The national survey of prostate cancer in the United States by the American College of Surgeons. *J Urol* 1982; **127**: 928.H2

APPENDIX

Counties[1] in the Five Planning Regions of Ontario[2]

NORTHWESTERN REGION	SOUTHWESTERN REGION	CENTRAL REGION	EASTERN REGION	NORTHEASTERN REGION
Kenora Rainy River Thunder Bay	Bruce Elgin Essex Grey Huron Kent Lambton Middlesex Oxford Perth	Brant Dufferin Durham (R.M.) Halidmand-Norfolk (R.M.) Haliburton Halton (R.M.) Hamilton-Wentworth (R.M.) Muskoka (D.M.) Niagara (R.M.) Northumberland Peel (R.M.) Peterborough Simcoe Toronto (M.M.) Victoria Waterloo (R.M.) Wellington York (R.M.)	Dundas Frontenac Glengarry Grenville Hastings Lanark Leeds Lennox and Addington Ottawa-Carleton Prescott Prince Edward Renfrew Russel Stormont	Algoma Cochrane Manitoulin Nipissing Parry Sound Sudbury (R.M.) Sudbury (T.D.) Timiskaming

[1] R.M. -Regional Municipality, D.M. - District Municipality, M.M. - Metropolitan Municipality, T.D. - Territorial District.

[2] Source : Ontario Ministry of Treasury and Economics, 1983.

LONG-RANGE PLANNING FOR CAPITAL NEEDS

R. GANDERTON, C.A.* and S. GATTESCO, C.A.*,
Toronto, Ontario

During the latter part of the 1980s, the demand for cancer care in Ontario grew at a rate which far surpassed the availability of capital and human resources. The 1980s delivered a clear message: Long-range planning is essential for the optimal delivery of cancer care in this province.

At the Ontario Cancer Treatment and Research Foundation (OCTRF), capital planning is the first step in developing a fully integrated overall plan encompassing capital, human resources, information systems and operating plans. The objective is an ongoing, comprehensive, planning process that allows us to deliver the appropriate range of cancer-care services in the right place and at the right time.

To develop the capital plan, two fundamental questions had to be answered:

1. How do we determine "demand" for future services?
2. How do we define the length of our planning cycle?

The first question forms the basis for our integrated planning exercise. In the paper "Cancer Incidence Projections for Ontario to the Year 2000", J. McLaughlin and W. King describe how statisticians make projections of cancer incidence. Using these projections, we forecast the number of patients who will require radiotherapy and chemotherapy and, based on established referral patterns, determine in which region these patients should be treated. These forecasts provide estimates of the demands for services which OCTRF must plan to meet.

The length of the planning cycle is critical; it must allow maximum flexibility so that we can adjust to changing circumstances and yet also have the long lead time required to plan, approve and construct or expand any new cancer care facility. At OCTRF the planning cycle is a continuum with a 10-year "horizon". By "continuum", we emphasize that once each year the plan is revised, looking 10 years into the future, to adjust the projections against current information on population, referral patterns, cancer incidence and modes of treatment. The 10-year span is ideal because:

- it allows for a planning horizon far enough in the future to ensure that we do not commit unneeded capital in the short term;
- it takes into consideration the 3 to 5 years needed to plan, approve and construct a facility;

---

*Interim management support at OCTRF, The Coopers and Lybrand Consulting Group, Toronto.

- it provides maximum lead time to ensure that we can meet operational and human resources needs.

Once these two fundamental questions were answered, we identified a host of other questions, such as:

1. What number of patients can be served with the resources available in the province today?
2. What standards of service delivery do we expect from our present capital investment, i.e. how many patients can a machine treat, how manysquare feet of physical space are required to accommodate patients, physicians and other health professionals?
3. What elasticity do our centres have to accommodate add-on facilities, i.e. new treatment machines, new clinical space construction?
4. What is the optimal size of a cancer centre? At what point is further expansion fiscally or operationally inefficient?
5. How to define a treatment day?

To be successful, any planning process requires the participation and support of the entire senior management group. At OCTRF all vice-presidents and the senior management groups at each cancer centre throughout the province have participated in the process. Specifically, we asked each vice-president for a "snapshot" of their present centres to estimate the following:

1. Present gross and net square footage of their respective centres;
2. The number of treatment machines on hand, their respective age, operational condition and technical status;
3. The centres' capacity to add clinical and support space and treatment machines and their special, shielded bunkers;
4. Capital equipment on hand other than direct radiation treatment machines and the age of that equipment;
5. Year of original construction plus each year when major renovations took place.

The data obtained in response to these questions and the incidence projections for the next 10 years formed the database on which we commenced the planning process.

Capital Planning

Capital planning can be subdivided into two equally important components: The quantitative and the qualitative processes. The quantitative is easily accommodated within any structural financial model. Using a common spreadsheet program, we quickly determined radiation machine and space requirements based on predetermined standards and the projections of cancer incidence.

Then we calculated machine requirements to determine their sensitivity to such variables as length of treatment day and projections of cancer incidence. There are other determinants of space but the number of radiation machines have a direct relationship to the physical size of any treatment centre. Assuming that the proportion of medical to radiation oncology "cases" remains constant, one can estimate the size of the building required to accommodate various patient loads. Even if this proportion varies within acceptable ranges, the size of any centre should not change substantially. Applying this quantitative exercise, we determined the provincial requirements for cancer treatment facilities for each of the next 10 years and compared this estimate to the individual "snapshot" of current resources. This showed us where and when we would require additional treatment facilities.

Each existing centre was modelled to expand up to its theoretical maximum capacity and we prepared a cost estimate which included machinery, equipment and renovation/construction costs in current-year dollars. In effect, the model takes the present system and, over a 10-year horizon, expands it to its maximum physical capacity. From this information and the projections of total incidence, we identified the shortfall in projected service capacity in the various regions of the province. This shortfall tells us where, when and how many new radiation machines, gross square feet and other capital resources will be required in the next 10 years. In addition, the long planning horizon allows us to build in an automatic "ability to expand" within these new centres. This provides a cost-effective and well-controlled growth environment which is sensitive to changing demographics and cancer-incidence projections.

The final stage of the quantitative analysis looks at replacement of existing equipment and replacement of new equipment put in place within the planning cycle. Based on our database plus the results of the initial stages of our quantitative analysis and predetermined useful life estimates, we established a replacement pattern that allows us to replace all equipment at the end of its useful life without compromising our ability to treat patients.

The quantitative phase of the planning cycle, although mechanical, is important nonetheless. It offers us a global overview and future-oriented perspective of OCTRF. In addition, such planning permits us to refine over time such things as types of equipment required, standardization of space and estimates of cost that take into account economies of scale. This is OCTRF's first attempt to model capital requirements and, although substantial progress has been made, we have only just begun.

The other component in planning is the qualitative process which operates as a constant check against quantitative analysis. The qualitative exercise imposes reality on the quantitative process. It looks at such issues as:

1. Is the planned expansion feasible within the projected time frame?
2. Are the host hospitals committed to the expansion required for a major cancer program?
3. Physically, can the host hospitals accommodate expanded cancer centre facilities?
4. Can we alter referral patterns to achieve optimal utilization of each cancer centre?

5. Does the projected expansion pattern make sense, i.e. is it economical to add one treatment machine per year for 4 years? For example, a more economical solution might be to build physical space in year X for 4 machines and phase in the required equipment.
6. Can we design optimal replacement patterns and then devise a better scale of priorities to guide their introduction?
7. Are the expansions and/or replacement patterns feasible in operational terms? For example, a centre that has 4 treatment machines could not replace 2 machines in a single year because it takes as long as six months to remove and install the new one.
8. Can we recruit human resources need to expand in the fashion projected?

The answers to these questions feed into our quantitative analysis and refines the capital forecast so that it provides a more realistic picture of OCTRF's needs.

In the last and most complex stage of capital planning, we ensure that the plan is not an isolated document. It must stand comparison with the organization's mission and goals. Fiscally it must respond to the funding available from the Ministry of Health and reflect the organization's own ability to raise its own share of the funding required. It must reflect the organization's future prospectives in terms of the level and types of care it intends to provide. It must also be fully integrated into the plans of the directors of human resources, operating and information systems. It must be consistent with and complementary to such initiatives as the Community Cancer Clinic Network and the province-wide Breast Screening Program. Equally important, the organization must identify the new programs and initiatives that will be undertaken over the planning cycle and try to understand and document their impact. This process is most complex and exciting because it requires not only the full co-operation and involvement of a host of interested parties but a visionary outlook.

At OCTRF the future is an exciting opportunity to initiate a planning process which will ensure for the people of Ontario the highest quality of cancer care possible. We will endeavour to work to continue to build our model and continuously refine it.

THE EVOLUTION AND DEVELOPMENT OF A COMMUNITY CANCER CLINIC NETWORK IN THE PROVINCE OF ONTARIO

J. GOWING, M.D.*,
Hamilton, Ontario

The community cancer clinic network (CCCN) dates back to the early radiotherapy follow-up clinics. As the number of the OCTRF Regional Cancer Centres grew and as the number of patients attending at these centres increased, thousands of patients were travelling long distances not only for treatment but also for examinations, consultations and for documentation of the progress of their disease. Therefore outreach clinics were established in community hospitals served by the Regional Cancer Centres and radiation oncologists travelled to the communities to serve these functions. With the introduction of systemic therapy to deal with what is in many instances a systemic disease, these therapies did not require the expensive equipment and setting required for radiotherapy. Private practitioners were able to administer many of these therapies in their local communities. The Regional Cancer Centres responded by introducing medical oncologists and converting follow-up clinics to more active treatment clinics; they also brought local internists/hematologists/oncologists into affiliation with the Centres. These affiliations have developed in a number of different ways, such as the Cancerlink Program at the Toronto-Bayview Regional Cancer Centre and the Oncology Outreach Program of the London Regional Cancer Centre and the Hamilton Regional Cancer Centre.

In 1985, as a result of a Provincial Role Study, the OCTRF set up an Ad Hoc Committee on Outreach and Chemotherapy. This Committee comprised representation from private practice, OCTRF Regional Cancer Centres, university teaching hospitals, the Oncology Section of the Ontario Hospital Association, and the Ontario Cancer Institute (OCI). A proposal for an ambulatory cancer care program entitled: "COMMUNITY CANCER CLINICS NETWORK" was presented to the OCTRF on April 8, 1987. Drs. J. Gowing, W.M. Hryniuk and J.W. Meakin continued to develop this proposal and sought advice and assistance from many jurisdictions including the Ontario Medical Association, the Ontario Hospital Association, other provincial health organizations and from countries such as Sweden, the U.K., Spain and the USA. During this time, a successful clinic was developed at Hotel Dieu Hospital in

---

*Medical Co-ordinator, Community Cancer Clinic Network, Hamilton Regional Cancer Centre; and Oncologist, Cambridge Memorial Hospital.

St. Catharines in co-operation with Dr. Brian Findlay and the Hamilton Regional Cancer Centre. The Oakville-Trafalgar Hospital has expressed interest in developing a clinic. Mr. Doug Carrothers, MPP, Oakville South, presented to the Legislature the following resolution on April 21, 1988: "That, in the opinion of this house, recognizing that cancer continues to be a major source of fatality in Ontario and recognizing the need for extensive research, diagnosis and treatment, the government of Ontario should support the development of a community based cancer clinic network".

On the same day the Executive of the Ontario Medical Association passed a resolution supporting the concept of CCCN. In June 1988, the Chairman of the Board of the OCTRF, Mr. Michael A. Meighen, presented a Proposal for a Community Cancer Clinic Network to the Minister of Health. In May 1989, at a combined meeting of senior management and Boards of the OCTRF and the OCI, this proposal was presented to the Deputy Minister of Health, Dr. Martin Barkin, and other Senior Ministry Officials. Dr. Barkin asked for an implementation plan to bring forward the CCCN proposal and to include a financial summary of phase-in costs. An Implementation Committee with expanded membership included representation from various health care constituencies of the province. The total committee includes 43 members. Five working parties were assigned to delineate a model description, implementation schedule, financial analysis, evaluation procedure, and a mechanism to facilitate liaison and promotion development. In April 1990, the Committee expects to submit a final document for Ministry consideration.

DESCRIPTION OF A COMMUNITY CANCER CLINIC NETWORK

Goals

The program would attempt to ensure the maximum cure rate for cancer and to ensure the delivery of quality care to the patient as close to home as possible.

To achieve these goals, the program would standardize service at a high level, provide a continuum of care, develop clinical research in the community, and develop a framework for cancer control.

Operational Model

The model is based on a network of community cancer clinics affiliated with a Regional Cancer Centre, recognizing their different needs depending on geographical location, population densities, access to resources and the nature of the facility (i.e. tertiary vs. nontertiary). This arrangement would be in the form of a partnership between the host hospital, the medical community, the Canadian Cancer Society and other appropriate agencies within the host community. Three levels of facilities are described dependent on the comprehensiveness of their treatment programs.

Community Cancer Clinic Level I

A Level I clinic would have a community cancer care advisory committee comprised of local physicians, hospital administrators, consumer groups, Canadian Cancer Society, home care, the Regional Cancer Centre and any other appropriate groups. This committee would provide advice on the development of the clinic.

Medical and/or radiation oncology services would be provided by consultants visiting from the Regional Cancer Centre or from a Level II clinic. A Level IB has been identified where a part-time local oncologist/hematologist might work with the visiting regional oncologist. Services would be co-ordinated by selected local physicians who would be designated as clinical associates. Nursing, pharmacy, social work, dietary and other support staff would be provided by the community hospital. The hospital would also provide diagnostic services such as laboratory and imaging services.

The Ontario Cancer Control Agency (OCCA), when established, would provide record keeping and data management using a uniform system specially designed for cancer care. Also OCCA would provide communication links, where appropriate.

Cytotoxic chemotherapy would be provided by a mechanism to be determined by all parties but subject to an annual revision.

Community Cancer Clinic Level II

A Level II clinic would have many of the arrangements of a Level I clinic including the appointment of clinical associates, support staff, diagnostic services, data management, chart keeping, communications and chemotherapy.

A major difference at Level II clinics would be the presence of an on-site, full-time medical oncologist. This would allow the delivery of more complex systemic treatments and for more triaging of patients referred to the Regional Cancer Centre. This method of diagnostic assessment is carried out in communities now but would be done in a more co-ordinated fashion under the direction of the visiting radiation oncologist. This would ensure that all patients have the opportunity for an appropriate referral. Therefore the radiation oncologist would provide consultation, limited follow-up, education, and research, as well as assisting in the development of the community clinic.

Surgical and gynecological oncologist also would play a major role in the development of multidisciplinary clinics within the community cancer clinics and in affiliation with the Regional Cancer Centres. The extent of this involvement will vary considerably from one community to another, particularly with regard to the consultant's expertise.

Because of their special character and resources, university teaching hospitals form a unique group of tertiary-care clinics; in this network they are designated as Level IIB clinics.

Community Cancer Clinic Level III

The Level III clinics are the existing Regional Cancer Centres including the Princess Margaret Hospital. Different categories of Level III (A to D) have been identified, contingent on the availability of special facilities and programs. Their most distinct function is that they are the sole facility for radiation therapy in the region that they serve. As leader in the region for treatment, research, training, education, early detection and prevention, they will facilitate a network of clinics within their own regions and throughout the province. This leadership will be most evident in the quality assurance and evaluation programs being developed in the context of the community cancer clinic network.

SUMMARY OF OCTRF EDUCATION ACTIVITIES

Postgraduate Medical Education

In 1989 the Foundation continued its support of postgraduate medical education by funding up to 20 residencies in oncology (medical or radiation) at an annual cost of approximately $800,000. The residency posts, which supplement those funded by the Ministry of Health in the five medical schools in the province, are an attempt to relieve the serious manpower shortage in these specialties.

Undergraduate Medical Education

The Ivan H. Smith Memorial Studentships

This program, jointly funded by the Canadian Cancer Society Ontario Division and the Foundation, provided 21 studentships in 1989 for periods of from 4 to 12 weeks. Competition for the studentships is open to medical students after their second year of study. At the OCTRF Regional Cancer Centres and the Princess Margaret Hospital, the Ivan Smith students are introduced to the rewarding aspects of a career in oncology. In 1989 participating centres were: Hamilton, Kingston, London, Ottawa, Thunder Bay, Toronto-Bayview, Windsor and the Princess Margaret Hospital. In 1990 the studentships can be held in pediatric oncology facilities at the Hospital for Sick Children (Toronto), the Children's Hospital of Eastern Ontario (Ottawa) and at the Regional Cancer Centres in Hamilton, Kingston and London.

The Harold E. Johns Summer Studentships in Medical Physics

In 1989, 13 studentships were taken in the following centres: Hamilton, Kingston, London, Ottawa, Thunder Bay, Toronto-Bayview and the Princess Margaret Hospital. This program, which is intended to stimulate the entry of medical physicists into oncology, is funded from a special cancer services improvement grant from the Canadian Cancer Society Ontario Division.

Continuing Medical Education

In 1989, staff members supported clinic days, seminars and guest lectures in the OCTRF Regional Cancer Centres and the Princess Margaret Hospital and gave lectures in the community.

During 1989, the Cancer Information Service continued to serve the public, patients, their families and friends, health professionals and the media across the entire province. This joint program of the Foundation and the Canadian Cancer Society Ontario Division is sited at the Hamilton Regional Cancer Centre. During 1990, the sixth year of its operation, it will undergo an on-site review by a team of Canadian and American experts. In keeping with new government policy, a bilingual Cancer Information Service must be put in place by 1991.

The 1989 visitor selected under the Joseph J. Schiffer Exchange Program was Dr. Harold Brenner, Chief of Oncology, the Chaim Sheba Medical Centre, Sackler School of Medicine, Tel-Hashomer, Israel. Dr. Brenner visited Toronto between October 5 and 13, 1989. This program, sponsored jointly by Mount Sinai Hospital and the Foundation, promotes scientific interchange between Israel and the University of Toronto health sciences facilities by supporting annual exchange visits of individuals working in the field of cancer care and/or research.

In 1989, there were two Ontario Cancer Foundation lectures. On June 22, at a meeting of the Network of Social Workers in Oncology at Queensway General Hospital, Dr. Francis J. Turner, former Dean of Social Work of York University, spoke on "A Changing Reality: The Impact of Multicultural Issues on Oncology Social Work". On October 14 at the annual meeting of the Ontario Association of Pathologists in Niagara-on-the Lake, Dr. D. Banerjee, Chief of Pathology, St. Joseph's Health Centre, London, Ontario spoke on "Flow Cytometry in the Evaluation of Lymphoproliferative Disorders".

On November 23, Dr. Janet Husband, Head, Department of Radiology, Royal Marsden Hospital, gave the Bert MacLaren Lecture at the Henderson General Hospital in Hamilton on "MRI in the Evaluation of Solid Tumors and Bone Marrow Malignancies".

The Ontario Cancer Treatment and Research Foundation/Canadian Cancer Society Ontario Division Educational Liaison Committee

This committee was formed in late 1989 to monitor the apparent overlap between the activities of the two organizations in public, patient and health professional education and to improve communication concerning these activities. The sponsoring bodies hope that, with improved communication, the two organizations can avoid duplication, give similar messages to the same target groups and launch joint endeavours in the future.

J.C. Laidlaw, M.D.

REGIONAL CANCER CENTRES

REGIONAL CANCER CENTRES

The Ontario Cancer Treatment and Research Foundation (OCTRF) was established in 1943 by an Act of the Ontario Legislature to conduct a program of research, diagnosis and treatment in cancer. The Foundation works in three fields: service, research and education. From its inception, the Foundation has accepted responsibility for:

- the establishment, maintenance and operation of research, diagnostic and treatment centres in general hospitals or special facilities; and
- the maintenance and operation hostels in connection with its treatment centres.

The Foundation also has the most important duty of co-ordinating facilities for cancer treatment and ensuring the adequate reporting of cases and the recording and compilation of data.

The Foundation with its eight Regional Cancer Centres – Hamilton, Kingston, London, Ottawa, Sudbury, Thunder Bay, Toronto-Bayview, and Windsor – provide facilities for undergraduate and postgraduate study, training of technical personnel, and research fellowships to increase our knowledge about cancer.

The Foundation is distinct from but co-operates with the Ontario Cancer Institute incorporating the Princess Margaret Hospital (OCI/PMH) in the investigation and treatment of cancer and works closely with the Canadian Cancer Society Ontario Division.

The Foundation hopes that Cancer in Ontario will assist the practising physician in some of the following ways:

- help him/her become familiar with the various services of the Foundation and its Centres;
- encourage effective patterns of referral and promote efficient geographical use of the Regional Cancer Centres;
- encourage the individual physician to consult informally with staff members at the Regional Cancer Centre;
- make the resources of the Foundation more widely available to the people of Ontario by increasing the number of contacts between physicians, particularly those outside metropolitan areas, and the OCI/PMH and the Foundation's Regional Cancer Centres.

We urge any physician who reads Cancer in Ontario to make suggestions concerning the improvement of cancer control in Ontario. These may be transmitted to the Chief Executive Officer (CEO) of the nearest Regional Cancer Centre or sent directly to the President, Dr. J.W. Meakin. The CEOs of the Regional Cancer Centres, who also are Vice-Presidents (VPs) of the OCTRF, may be contacted as follows:

OCTRF Head Office
Dr. J.W. Meakin – President and Chief
Executive Officer, OCTRF
7 Overlea Blvd.
Toronto, Ontario M4H 1A8
Telephone: (416)423-4240

Hamilton Regional Cancer Centre (HRCC)
Dr. W.M. Hryniuk – Chief Executive
Officer HRCC and
Vice-President OCTRF
Henderson General Hospital
711 Concession Street
Hamilton, Ontario L8V 1C3
Telephone: (416)387-9495

Kingston Regional Cancer Centre (KRCC)
Dr. A.D. Ginsburg – Chief Executive
Officer KRCC and
Vice-President OCTRF
Kingston General Hospital
King Street West
Kingston, Ontario K7L 2V7
Telephone: (613)544-2630

London Regional Cancer Centre (LRCC)
Dr. L. Levin – Chief Executive
Officer LRCC and
Vice-President OCTRF
Victoria Hospital
790 Commissioners Rd. E.
London, Ontario N6A 4L6
Telephone: (519)685-8600

Northeastern Ontario Oncology Program
(NEOOP)
Dr. R.E.T. Corringham – Chief Executive
Officer NEOOP and
Vice-President OCTRF
Laurentian Hospital
41 Ramsey Lake Road
Sudbury, Ontario P3E 5J1
Telephone: (705)522-0454

Ottawa Regional Cancer Centre (ORCC)
Dr. W.K. Evans – Chief Executive
Officer ORCC and
Vice-President OCTRF
Civic Hospital Division
190 Melrose Avenue
Ottawa, Ontario K1Y 4K7
Telephone: (613)725-6300

General Hospital Division
501 Smyth Road
Ottawa, Ontario K1G 8L6
Telephone: (613)737-7700

Thunder Bay Regional Cancer Centre
(TBRCC)
Dr. J.F. Kotalik – Chief Executive
Officer TBRCC and
Vice-President OCTRF
General Hospital of Port Arthur
290 Munro Street
Thunder Bay, Ontario P7A 7T1
Telephone: (807)343-1610

Toronto-Bayview Regional Cancer Centre
(T-BRCC)
Dr. R.D.T. Jenkin – Chief Executive
Officer T-BRCC and
Vice-President OCTRF
Sunnybrook Medical Centre
2075 Bayview Avenue
Toronto, Ontario M4N 3M5
Telephone: (416)488-5801

Windsor Regional Cancer Centre (WRCC
Dr. G.C.K. Mok – Chief Executive
Officer WRCC and
Vice-President OCTRF
Metropolitan General Hospital
2220 Kildare Road
Windsor, Ontario N8W 2X3
Telephone: (519)253-5253

OCF

HAMILTON REGIONAL CANCER CENTRE

HENDERSON GENERAL HOSPITAL

Chief Executive Officer:

W.M. Hryniuk, M.D.

Radiation Oncologists:

V.R. Basrur, Ph.D., M.D.
D.I. Hodson, M.B., B.Ch.
C.R. Johanson, M.D.
G. Jones, M.D.
H. Lukka, M.B., Ch.B.
J. Sathya, M.B., B.S.
I.Z. Strautmanis, M.D. (to July/89)
A.A.M. Tadros, M.B., B.Ch.
A. Whitton, M.B., B.S.

Medical Oncologists:

A. Arnold, M.B., B.S.
G.P. Browman, M.D.
E. Chouinard, M.D.
A.T. Figueredo, M.D.
H. Hirte, M.D.
M.N. Levine, M.D.
P.B. McCulloch, M.D.
A.J. Neville, M.B., Ch.B.
J.J. Rusthoven, M.D.

Gynecologic Oncology:

G. O'Connell, M.D.
J. Mazurka, M.D.

Physicists:

C. Kwok, Ph.D.
C. Lewis, M.Sc.
M. Patterson, Ph.D.
V.G. Peters, M.Sc.
R.H. Price, B.Eng.
B.C. Wilson, Ph.D.
D. Wyman, Ph.D.

Clinical Assistants:

N. Frape, M.D.
H. Geffen, M.D.
M.D.E. Goodyear, M.B., B.S.
E. Latimer, M.D.
M.E. McBride, M.D.
D. Nicholson, M.B., B.Ch.
C.L. Tanser, M.D.
D. Ward, M.D.
J. Witcher, M.D.

Career Scientists:
G. Singh, Ph.D.

Administrator:
C.E. Squires

Business Office Manager:
C.F. Freeman, R.I.A.

Senior Radiotherapy Technologist:
B.J. Walker, R.T.

Nurse Administrator:
G. Holmes-Brown, R.N., B.A.S.

Cancer Information Service:
B. Rigby, B.Sc.N., M.H.Sc.

Manager of Health Records:
D. Armstrong

Lakeview Lodge Supervisor:
C. Dawson, R.N.

1989 was a significant year in the development of the new Hamilton Regional Cancer Centre. Site preparation began in August and, in September, a ground-breaking ceremony was held. Mr. Michael Meighen was the host and Premier David Peterson gave the keynote address. Representatives attended from the various regional and hospital constituencies, the Canadian Cancer Society and the Ontario Cancer Treatment and Research Foundation. A scale model of the new Centre was displayed later at a reception in the Henderson General Hospital. In December, tender bids for the main project were forwarded to the Ontario Ministry of Health for review and approval.

To meet the challenge of providing sufficient oncology manpower, we have increased enrollment in our undergraduate and postgraduate training programs. The Radiation Therapy Department has taken in more radiation technology students under the clinical instructorship of Marcia Taggart, RT. At present, five residents are enrolled in the postgraduate programs of radiation and medical oncology. This year, Dr. Alan Neville became director of postgraduate training in medical oncology and also was appointed Director of the McMaster Clinical Teaching Unit (internal medicine) at our host hospital, the Henderson. In the Nursing Department, Mrs. June Scruton has accepted the post of nurse administrator for education and research. In December, Michael Fraumeni was appointed librarian of the new Centre.

In July, the staff of the Centre said "farewell" to two of its senior members: At a retirement party for Dr. Ingrid Strautmanis they recognized her 20 years of dedicated service to the Department of Radiation Oncology; Anne Devries has resigned as librarian after serving for 12 years.

The Department of Radiation Oncology welcomes Dr. Glenn Jones, who has completed a one-year fellowship in the postgraduate program under Dr. Whitton. Dr. Jones will combine his laboratory and clinical interests as he works with Dr. Brian Wilson in the study of photodynamic therapy in specific disease sites. Dr. Jones becomes the first member from the department to enroll in McMaster University's Masters Program of Design, Methodology and Evaluation. This experience in methodology and design will assist the department in the development of clinical trial protocols.

The Department of Medical Oncology welcomes Dr. Hal Hirte, who is the first clinician-scientist to be appointed to the Hamilton Centre. Dr. Hirte will set up an independent research program to study the application of biologic response modifiers to the treatment of ovarian cancer.

The Surgical Oncology Service welcomes Dr. John Mazurka, who joins Dr. Greg O'Connell; he will make a significant contribution to patient care and teaching in the Department of Gynecologic Oncology.

On July 1, 1989, Dr. George Browman became the Chairman of the Department of Clinical Epidemiology and Statistics at McMaster University. During his tenure, he will continue his clinical practice at the Centre and participate in collaborative research studies at the national and local levels.

In April, Dr. Mark Levine, Head of the Department of Clinical Trials at the Hamilton Centre and Co-ordinator of the Ontario Clinical Oncology Group, was named a research scientist of the Medical Research Council of Canada. He was the first clinician to receive this award.

Dr. William Hryniuk and Ms Barbara Rigby received the 1989 Public Service Award from the Canadian Women's Breast Cancer Foundation at a ceremony held in Toronto on October 17, 1989. The award recognized their work in establishing the joint Provincial OCTRF/CCS Cancer Information Service. Dr. Hryniuk is serving the second of a three-year appointment to the Board of Scientific Counselors in the Division of Cancer Treatment at the National Cancer Institute in Bethesda, Maryland. He continues to foster collaborative research into the treatment of Stage IV breast cancer; specifically, into the appropriate dose intensity of various chemotherapeutic agents. In the past year, Dr. Hryniuk has been an invited speaker at the Third International Conference on Adjuvant Therapy of Breast Cancer in St. Gallen, Switzerland; the Fourth World Conference in Clinical Pharmacology, Heidelberg, Germany; and at the Joint NCI-IST Symposium in Genoa, Italy.

In May, the Canadian Medical Association presented Dr. Elizabeth Latimer, a consultant in psychosocial/supportive care, with the 1989 Osler Scholarship. In July 1989, Dr. Latimer began a six-month sabbatical to pursue further studies in palliative care.

In July, Dr. Brian Wilson, Director of Research and Head of Physics at the Hamilton Centre, was honored by a permanent appointment as a Visiting Professor to Wellman Laboratories of Photomedicine, Harvard Medical School. Dr. Wilson commutes between Hamilton and Boston to discharge his many commitments. Under his directorship, our Centre has made a significant contribution to collaborative studies of laser applications at both the basic and clinical levels. Dr. Wilson and his colleagues, Drs. Michael Patterson and Douglas Wyman, recently obtained a grant of $100,000 to support research into new medical applications of laser energy. This continuing grant is administered by the Ontario Laser and Lightwave Centre, a provincially-supported Centre of Excellence, based at the University of Toronto. In addition, these scientists participate in a formal multicentre research collaboration for the investigation of optical diagnostics and tissue spectroscopy using laser facilities at the Massachusetts Institute of Technology, the Harvard Medical School, and the M.D. Anderson Hospital.

The academic programs of our Centre continue with a generous grant from Adria Laboratories. During this past academic year, the Thursday regional oncology rounds were addressed by five visiting professors. This postgraduate event, which addresses the needs of a wide variety of subspecialties and disciplines, is open to all professionals. The monthly, clinical-trials dinner, which continues into its eleventh year, provides our investigators with valuable information through audits of current treatment practices.

In April 1990, under the direction of Dr. Martin Barkin, Deputy Minister of Health, a joint task force of the Ontario Cancer Treatment and Research Foundation and the Ontario Ministry of Health will develop a plan to implement a community cancer clinic network (CCCN) for the Province. A subcommittee made up of Drs. William Hryniuk and James Gowing, and Ms Heather M. Hiscox will ensure that the Implementation Committee will complete its deliberations and submit its report before the end of the fiscal year 1989-90. The main committee of 34 members represents several regional cancer centres and provincial health care organizations. It will identify costs of implementation, proposed sites for clinics and define the role to be assigned by the regional cancer centres. A complete description of the CCCN may be found elsewhere in this issue.

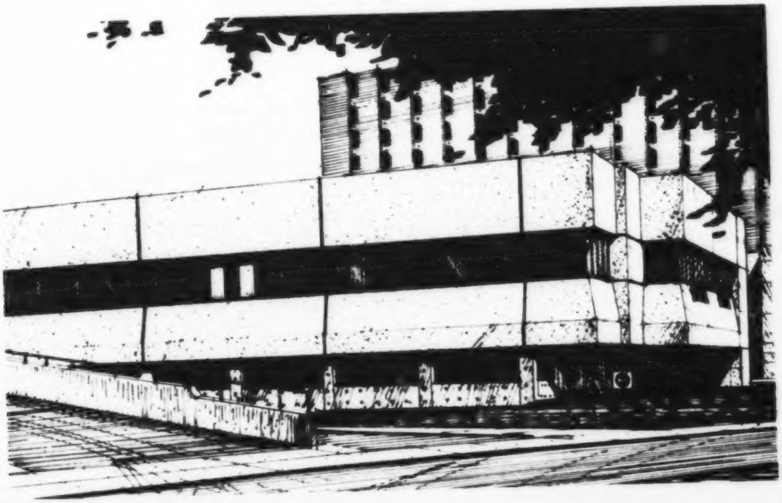
On May 4, the Ontario Ministry of Health awarded funds to establish a Provincial Breast Cancer Screening Program. Hamilton will be one of the eight screening centres. Joint Community Committees have been established in Hamilton and London to assist in the organization of these centres. We expect the first centre to open in the Spring of 1990.

During the next two years, the Hamilton Centre's resources will be further strained while we await the completion and occupation of our new facility. The new structure, which will be five stories high and will provide approximately four times our present space, will enable us to provide treatment, research and teaching appropriate to a tertiary cancer care centre.

Heather M. Hiscox
Administration

KINGSTON REGIONAL CANCER CENTRE

KINGSTON GENERAL HOSPITAL



Chief Executive Officer:
A.D. Ginsburg, M.D.

Radiation Oncologists:
M. Brundage, M.D.
P.F. Dixon, M.B., B.S.
P.J. Froud, M.B., Ch.B.
V. Kraus, M.D.
W. Wells, M.D.

Medical Oncologists:
B.J. Campling, M.D.
E.A. Eisenhauer, M.D.
P.R. Galbraith, M.D.
W.S. Lofters, M.D.
J.L. Pater, M.D.

Clinical Assistants:
M.D. Mulligan, M.R.C.S., L.R.C.P.
P. O'Donnell, M.D.
D.C. Pross, M.D.

Career Scientists:
S.P.C. Cole, Ph.D.
J.S. Gerlach, Ph.D.
J.C. Kennedy, M.D.

Physicists:
J. Robins, M.A.
P.C. Shragge, Ph.D.
J. Szabo

Honorary Medical Consultant:
R.C. Burr, M.D.

Administrator:
TBA

Head Nurse:
A. Voino, R.N.

Chief Technician:
N. Hobbs

Social Service Nurse:
C. Keith, Reg.N.

Manager of Health Records:
R. MacDonald, C.C.H.R.A.(C)

Quinte-Thousand Island Lodge Supervisor:
D. Broeders, Reg.N.

The past year has seen a dramatic increase in the number of patients referred to our Centre. In response to staff and equipment shortages in Toronto we proposed an increase in our catchment area to include patients from the Counties of Peterborough, Durham, Victoria, Northumberland and Haliburton. In this initiative, we had the enthusiastic support of the Kingston General and Hotel Dieu Hospitals, and Queen's University. Ministry of Health supported us with a sizable increase in our operating budget. The entire staff has responded with selfless dedication to facilitate the care of all our patients – new and old. Indeed, several recent glowing newspaper articles attest to patient acceptance and satisfaction.

Recognizing that these new referral patterns may be difficult for the physician, we produced a brochure which describes the personnel and functioning of the Centre and distributed it to all physicians in the "Five Counties".

To facilitate communication with referring physicians we are developing protocols outlining the approach taken at our Centre and Health Sciences Complex to the treatment of specific tumors. These protocols, which are being prepared in consultation with physicians from many departments in the Faculty of Medicine at Queen's University, are available to area physicians on request. We shall appreciate comments and constructive criticism. As part of our policy of setting treatment guidelines, we have initiated a series of prospective and ongoing audits to measure the effectiveness of these policies. These too are available on request.

Under the stewardship of Dr. John Carmichael, and with the strong support of the Departments of Surgery, Gynecology, Urology and Otorhinolaryngology and the Faculty of Medicine, and in keeping with our philosophy of multidisciplinary cancer care, we are developing a division of surgical oncology in the Department of Oncology at Queen's University. The object is to enhance patient care by the institution, in the first instance, of multidisciplinary, site-specific conferences. Area physicians are welcome at these conferences.

The nurses have organized a weekly "psychosocial" conference to enhance the patient's supportive care. These are well-attended by our own staff and also by several psychiatrists, psychologists, the hospital chaplaincy and several social workers. We believe that supportive care is as important to the care of the cancer patient as is the more technical care we provide. This conference is a step towards the co-ordination and enhancement of the various valuable services in this sphere available to our patients. Also we are eager to undertake appropriate behavioural research, which will enhance cancer care.

Basic research is flourishing under the direction of Dr. Roger Deeley. Recently, he and his group received a major award from the National Cancer Institute of Canada – a fitting tribute to the quality of their work.

These are challenging times for cancer care. We are pleased to have the opportunity to respond.

A. David Ginsburg, M.D., F.R.C.P.(C)
Chief Executive Officer

LONDON REGIONAL CANCER CENTRE

VICTORIA HOSPITAL

London Regional Cancer Center

Chief Executive Officer:
L. Levin, M.D.

Radiation Oncologists:
A.R. Dar, M.B., B.S.
B. Fisher, M.D.
L.E. Gaspar, M.D.
J.A. Hammond, M.D.
A.L. Houghton, M.B., Ch.B.
F. Perera, M.D.
A.T. Porter, M.D.
H.L. Prichard, M.B., B.S.

Medical Oncologists:
V. Bramwell, M.B., B.S.
G. Cairncross, M.D.
W.I. Kocha, M.D.
R.C. Lohmann, M.D.
D. Macdonald, M.D.
W. Mertens, M.D.
J. Skillings, M.D.
T.A. Vandenberg, M.D.

Physicists:
A. Akinradewo, Ph.D.
R. Barnett, Ph.D.
J. Battista, Ph.D.
D.J. Dawson, Ph.D.
P. Munro, Ph.D.
J. Schroeder, M.Sc.

Career Scientists:
A. Chambers, Ph.D.
G. Hammond, Ph.D.
J. Harris, Ph.D.
W.R. Inch, Ph.D.
D.J. Koropatnick, Ph.D.

Administrator:
B. Paulse, M.H.A.

Business Manager:
B. Hodgert, B.A.

Nursing Services Acting Manager:
E. Anderson, M.Sc.N.

Radiation Therapy Technology Manager:
P. deSilva, R.T.T.

Social Work Manager:
A. Sawarna, M.S.W.

Health Information Services Manager:
D.G.E. Ross, C.C.H.R.A.

Thameswood Lodge Manager:
C. Sellery, B.Sc.N.

The past year at the London Regional Cancer Centre (LRCC) has been a period of consolidation coupled with sustained growth in research and oncology education. During this period three additional cancer research laboratories were constructed bringing the total to nine; there are also two physics research laboratories. Dr. Geoff Hammond is the new director of the cancer research laboratories. Victoria Hospital have provided additional funding for this effort. We anticipate that, in the near future, the Faculty of Medicine, University of Western Ontario (UWO), will fund a further scientist position through the Department of Gynecology. The Departments of Physics and Radiation Oncology are conducting research in portal imaging, experiments with new sealed and unsealed radioactive sources and 3-dimensional treatment planning. Also, ground has been laid for a brachytherapy program under the guidance of Drs. Artur Porter and Jerry Battista; some of this research is being done in conjunction with the Robarts Research Institute. Shortly, the London Centre hopes to complete its one-year probation with the RTOG (radiation therapy oncology group) thereby becoming a full member. Industrial grants and MRC funds provide the chief support for radiation oncology and physics research but we hope this will be supplemented by RTOG funds in the coming year.

Dr. Vivian Bramwell has completed her three-year term as Director of the Clinical Studies Unit. Under her guidance, this unit has become increasingly effective and continues to drive a multitude of clinical research activities. Dr. Jamey Skillings, who succeeds Dr. Bramwell as director, will continue this important activity.

The Oncology Education Program has grown rapidly in the past year. With the help of the LRCC staff, Shelley Markland has set up numerous workshops for health-care professionals across Southwestern Ontario. Thus the expertise generated at the Centre is disseminated to community-based agencies thereby enhancing the quality of patient care. The LRCC sponsored a highly successful public lecture series and, more recently, also conducted a patient education series. We have produced video tapes covering such subjects as radiotherapy, chemotherapy, pain control, palliation, psychosocial support, and an introduction to Thameswood Lodge. These tapes have been disseminated across the region and many patients have seen them usually before they come to London for treatment. A highlight of the Oncology Education Program was the launching of ONCORE, a journal to educate health-care professionals about cancer prevention, treatment and palliation. This, the first journal of its kind, is being distributed across Canada. We will continue to publish ONCORE as a quarterly journal.

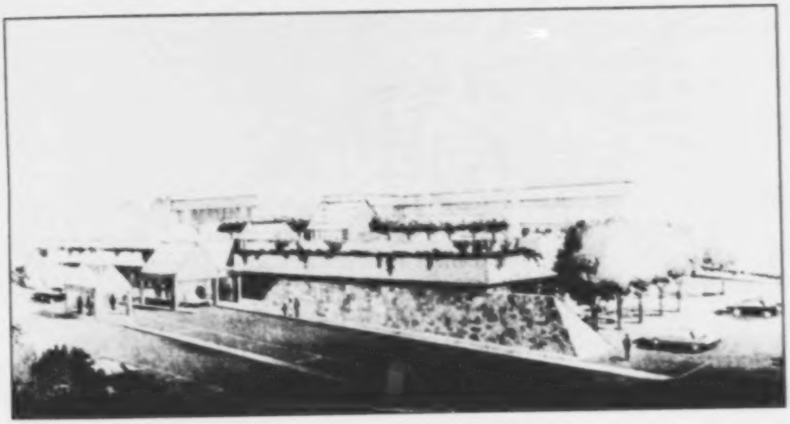
During the past year, Mary Jean Morrison, our administrator, moved to Toronto to become planning co-ordinator at the Princess Margaret Hospital. Although we will miss Mary Jean, we are pleased that she will remain in the cancer care "family". Our new administrator, Mrs. Bertha Paulse, will add significant strength to the administrative infrastructure needed by an expanding centre. We bid farewell to Dr. Peter Corbett who moved to Calgary. Dr. Arthur Porter is now Head of the Department of Radiation Oncology and Head of the Division of Radiation Oncology, UWO. Drs. Barbara Fisher and Francisco Perera joined our staff during the last year as radiation oncologists and Dr. Ted Vandenberg joined the St. Joseph's Hospital-LRCC Oncology Unit as a staff medical oncologist. We also welcome Dr. Rob Barnett to our physics department.

We, at the LRCC, are grateful that we have a beautiful new facility to work in. Our staff continued to work hard to ensure a high quality of patient care, research and education. They will continue along these lines during the coming year.

Leslie Levin, M.D.
Chief Executive Officer

NORTHEASTERN ONTARIO ONCOLOGY PROGRAM

LAURENTIAN HOSPITAL, SUDBURY



Chief Executive Officer:
R.E.T. Corringham, M.B., B.S.

Radiation Oncologist:
R.J. Bissett, M.D.
P.D. Lefebvre, M.D.

Medical Oncologists:
C.J. Germond, M.B., B.Ch.
G.D. Goss, M.B., B.Ch.
C.L. Sinoff, M.B., B.Ch.
M.D. Vincent, M.B., Ch.B.

Clinical Assistant:
G.M. Kane, M.B., B.Ch.

Epidemiologist:
V. Nguyen, Ph.D.

Psychologist:
S. Steggles, Ph.D.

Nurse Administrator:
C. McChesney, B.Sc.N.

Manager of Health Records:
R. Zambelli, C.C.H.R.A.(C)

After a quiet summer, the new Centre building is in the final phase of construction and should be closed in before winter. We anticipate that the building will be completed early, ahead of the scheduled completion date of December 1990. As the pace of construction increases, so do the many other elements of the Northeastern Ontario Oncology Program (NEOOP), including equipment purchase and recruitment of additional staff. Ms. Christine Chadwick has been appointed project co-ordinator, and, in a reorganization of NEOOP's administration, Mrs. Monique Poirier has become our new business manager. We now have a senior management team, a unique form of administration within the Foundation, and it appears to be well suited to our energetic and rapidly developing organization.

In October, in a joint ceremony, the Hon. Elinor Caplan, Minister of Health, and the Hon. Rene Fontaine, Minister of Northern Development, opened the new Collaborative Cancer Research Laboratories at Laurentian University and unveiled a commemorative plaque marking the cornerstone of the new Centre. In Sudbury, laboratory-based cancer research is a joint venture between the Laurentian University and NEOOP. Dr. Anthony Ho, a clinician scientist, has been appointed NEOOP's first director of research and will arrive from the University of Heidelberg in the new year. The Ministry of Northern Development have assisted this project with a $1 million start-up grant.

The clinical program continues to grow and is entering increasing numbers of patients into clinical trials. As well as participating in NCIC and NSABP studies, NEOOP also conducts its own small-cell lung cancer trial in collaboration with the Thunder Bay Regional Cancer Centre. These results were presented at both the American Society of Clinical Oncology meeting in San Francisco and the 5th European Conference on Clinical Oncology in London, England. Among new staff, we welcome Drs. Colin Germond and Pierre Lefebvre, and Carole Aubut, our new social worker. With regret, we said "goodbye" to Dr. Thomas Bozek, who having failed to obtain accreditation from the Royal College of Physicians and Surgeons of Canada returned to England to take a consultant post at Guy's Hospital, London.

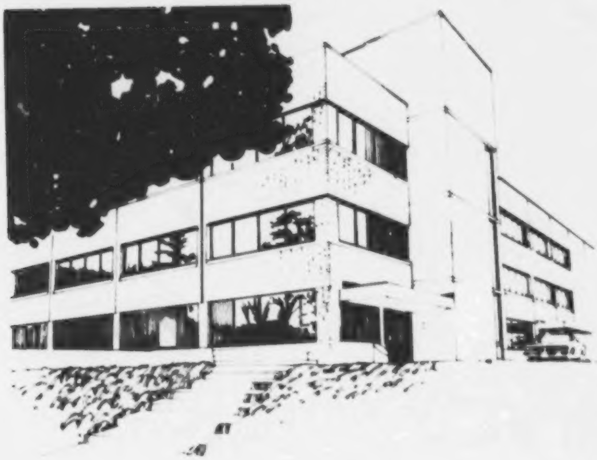
As the Centre nears completion, excitement is rising. NEOOP staff have a challenging year ahead and there is much yet to do before the opening of the new Centre. In view of the present shortfall in radiation services in this province, particularly for residents of the North, the new Northeastern Centre in Sudbury has metamorphosed from being what some skeptics believed would become a "white elephant" to being a "white knight". Once again the NEOOP staff have demonstrated their enthusiasm, dedication and hard work in helping cancer patients and in further developing the Program. With the opening of the Centre next year, we look forward to joining the other regional cancer centres as an equal partner in the provincial cancer-care network.

R.E.T. Corringham, M.B., B.S.
Chief Executive Officer

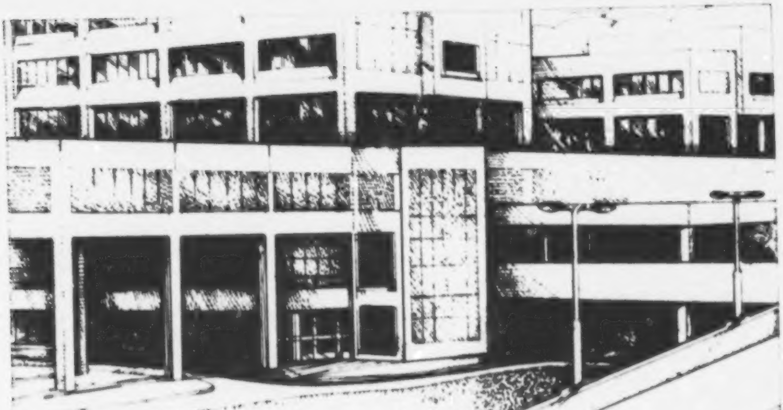
OCF

OTTAWA REGIONAL CANCER CENTRE

OTTAWA CIVIC HOSPITAL



AND OTTAWA GENERAL HOSPITAL



Chief Executive Officer:
W.K. Evans, M.D.

Radiation Oncologists:
J. Crook, M.D.
C.J.E. Danjoux, M.D.
L. Eapen, M.D.
B. Esche, M.D.
P. Genest, M.D.
A.L. Girard, M.D.
L. Grimard, M.D.
B.D. Nair, M.B., B.S.

Medical Oncologists:
S. Aitken, M.D.
C. Cripps, M.D.
D. Logan, M.D.
J.A. Maroun, M.D.
D.J. Perrault, M.D.
D.J. Stewart, M.D.
S. Verma, M.D.
V.P.J. Young, M.D.

Clinical Assistants:
H. Bastianelli, M.D.
M. Carew, M.D.
P. Craigie, M.D.
S.Gertler, M.D.
S. Langlois, M.D.
K. O'Toole, M.D.
I.A. Prosser, M.D.
M. Reed, M.D.
K. Robillard, M.D.
M. Touchie, M.D.
S. Wong, M.D.

Career Scientists:
H.C. Birnboim, M.D.
R.G. Liteplo, Ph.D.
R. Hawley, Ph.D.

Physicists:
I. Cameron, Ph.D.
J. Cygler, Ph.D.
L.H. Gerig, Ph.D.
G.P. Raaphorst, Ph.D.
D. Salhani, Ph.D.
M. Soubra, M.Sc.
J. Szanto, Ph.D.

Administrator:
M.L. Trickey, M.B.A.

Business Manager:
E.J. O'Reilly, C.M.A.

Executive Secretary:
D. Pineau, C.M.S.

Nurse Administrator:
C.J. MacMillan, B.Sc.N.
(to Sept. 15/89)
B. Skinn, B.Sc.N.
(from Sept. 16/89)

Head Nurse (General Division)
L. Fawcett, R.N.

Head of Radiation Technologists:
R.P. Wallace, A.C.(T)

Managers of Health Records:
Civic Hospital Division
S.A. Parsons, C.C.H.R.A.(C)
General Hospital Division
M.M. Brassard

Lodge Managers:
J.M. Davidson, R.N.,
(Maurice J.Grimes Lodge)
I. Martin, R.N.,
(Pavillon Alta-Vista Lodge)

The past year has seen many changes at the Ottawa Regional Cancer Centre. Among the priorities of its new Chief Executive Officer, Dr. W.K. Evans, have been: The development of a mission statement; refinement of the Centre's organizational structure; recruitment of new staff, and renovations at both the Civic and General Divisions to optimize function. Dr. Jean Maroun is the new head of medical oncology for the Centre. He brings to his new position well-recognized talents in clinical research, administration and teaching as well as an ample sense of humor. Dr. David Stewart, who has become head of medical oncology at the Civic Division, has moved his pharmacology research program from the Ottawa General Hospital to the research laboratories in the Civic's cancer facility. David brings to his job a high energy level, an encyclopedic knowledge of oncology and a remarkable dedication to clinical research. Dr. Susan Aitken has moved her office to the General Division of the Centre. Dr. Diane Logan, the Centre's clinician scientist, has established her laboratory within the Ottawa General Hospital.

The Ottawa Centre was sad to see Dr. Betty McDermot retire in December 1988. For 28 years, Betty has served the Centre as a teacher, clinical investigator and a caring and compassionate physician. She will be much missed. However, Dr. McDermot has only retired partially and maintains an association with the Centre through an outreach clinic at the Queensway-Carleton Hospital. Here she can follow-up many of the patients she had treated earlier. In January 1989, Dr. Laval Grimard joined radiation oncology after a year of subspecialization in France with Professor Pierquin in brachytherapy and Mr. Jean Louis Habrand in pediatric oncology. Dr. Grimard's appointment further strengthens the Centre's already strong brachytherapy program. He will work with Drs. Juanita Crook, Bernd Esche and Paul Genest. The Ottawa Centre offers expertise in stereotactic radioactive brain implants, intraluminal brachytherapy for cancer of the esophagus, and interstitial implants for breast, oropharyngeal and rectal cancer.

Dr. Doug Salhani, who joined the physics department recently, brings expertise in mathematical modelling and computers. During the year he helped to commission and bring into operation the new KD-2 linear accelerator at the General Division. In future, Doug will take a particular interest in the research program in dynamic radiotherapy.

The Centre's residency training programs have attracted a number of recruits. Drs. John Radwan and Salim Chammas entered the radiation oncology program and Dr. Gerry Thomas began the medical oncology program.

Several new clinical assistants have arrived to help with the increasing outpatient load. At the General Division, Dr. Michael Touchie works with the medical oncologists and recently we recruited Dr. Stan Gertler to assist with inpatients at the Civic Division. Dr. Pamela Craigie is the first inpatient clinical assistant at the General Division.

We have strengthened the psychosocial support for cancer patients by the addition of Dr. Mary Navarro, a psychiatrist, to the consultant staff. Dr. Navarro will provide consultative service to our outpatients. Mr. Ralph van der Hoek, an Ottawa Civic Hospital social worker, will work closely with the radiation oncology staff to provide psychosocial support to both inpatients and outpatients.

There have been substantial changes among our support staff. Mrs. Susan Parsons brings great experience and expertise to her new position as manager of health records at the Civic Division. Previously Susan was head of medical records at the Joseph Brant Hospital in Burlington. Thomas Wadsworth is the new computer manager for the Centre. Formerly he had been with the Ontario Ministry of Education and has substantial knowledge of the hardware platform and software programs required for the new OPIS system. In September 1989, Barbara Skinn became nurse administrator for the Centre. Barbara has a Master's degree in nursing and previous experience in the OCTRF system; she had worked in the Hamilton Regional Cancer Centre's outreach centre in Cambridge. Barbara replaces Cora MacMillan who retired after 12 years of strong nursing leadership. We wish Cora well in her retirement. Earl O'Reilly has been appointed financial services manager for the Centre effective October 1989. Earl, who has a B.Comm. degree and a C.M.A., will bring strength and stability to financial services at the Centre.

In 1989, Drs. Kate Lochrin and Pierre Lefebvre completed their residency training in radiation oncology and both passed the Royal College Fellowship examinations. Dr. Lefebvre has joined the staff of the Northeastern Ontario Oncology Program in Sudbury and at present is serving patients from the Northeastern Ontario at the Princess Margaret Hospital in Toronto. Dr. Lochrin is continuing her postgraduate training with Dr. S. Dishe at the Mount Vernon Hospital in Northwood, Middlesex, England.

The radiotherapy technology training program, which earlier could accommodate only three students each year, now can accommodate up to eight trainees. In October, James McLellan, Cheri Gaddess and Jeanette Rintoul graduated from the training program and joined the staff at the Centre. Mr. Steve Andrusyk and Mrs. Sally Grimes have been awarded advanced certification by the Canadian Association of Radiation Technology.

Several members of our staff achieved notable distinctions during the past year. The Centre takes particular pride in the honor bestowed on Dr. S.E. Aitken, Lt. Col. (Ret.). In June the Governor General, Jeanne Sauve, awarded her the Order of Military Merit in recognition of her efforts in establishing a section of medical oncology within the National Defence Medical Centre.

We congratulate Mrs. Wanda Assang for the completion of her Master's degree in Nursing.

The Centre hosted a number of distinguished visitors during the past year: On December 13, 1988, Dr. Carolyn Freeman from McGill University discussed "Brain tumors in children"; and on January 31, 1989, Dr. Simon Sutcliffe from the Ontario Cancer Institute made a presentation on "Infertility in cancer patients". In addition, Dr. M.A. Epstein of the University of Oxford, recipient of the 1988 Gairdner Foundation International Award for the identification of the Epstein-Barr virus, discussed on October 17, 1988 the Epstein-Barr virus and malignancy. City-wide oncology rounds were enriched by presentations by: Dr. Armand Keating on bone marrow transplantation in Hodgkin's disease, on September 20, 1988; by Dr. Donald Abrams from San Francisco on AIDS-related malignancies, on April 25, 1989; and by Dr. Vivian Bramwell from the London Regional Cancer Centre on the management of soft-tissue sarcomas, on December 13, 1988.

The Centre's physicians, physicists and scientists have shared the results of their research activities at local, national and international meetings. In Florida, in November 1987, Dr. W.K. Evans spoke at a workshop of the International Association for the Study of Lung Cancer on non-small-cell lung cancer. In June of 1989, he was invited to speak at the Second IASLC Workshop in Elsinore, Denmark, on small-cell lung cancer. Also he was an invited speaker at a symposium on lung cancer in June 1989 in Saskatoon and in October 1989 in Indianapolis. At a symposium on nutrition in Kingston he described the nutritional support of the cancer patients and participated in a workshop on dietary carcinogens. Finally, in August 1988, Dr. Evans was a plenary session speaker on adjuvant therapy for surgically resected lung cancer at the Fifth World Conference on Lung Cancer in Interlaken, Switzerland. Also at the Fifth World Conference on Lung Cancer in Interlaken, Switzerland, in August 1988, Dr. Jean Maroun described his randomized trial of radiation therapy with or without lonidamine.

At an international symposium on hyperthermic oncology in Kyoto, Japan, in August 1988, Dr. Lee Gerig described his work on the measurement of blood flow by thermal wash-out during microwave hyperthermia.

On March 30, 1988, Dr. David Stewart gave a paper on investigational chemotherapy of brain tumors at the Memorial Sloan-Kettering Cancer Center in New York and on April 14, 1988, participated at a symposium entitled "Interferons: Yesterday, Today and Tomorrow" in Nassau, Bahamas. Also he gave a paper on the role of clinical pharmacology in cancer treatment at the University of Hawaii, in Honolulu in January 1989. In June 1989, he attended the 16th International Conference of Chemotherapy in Jerusalem, Israel and spoke on neurotoxicity as part of a symposium entitled "Chemotherapy Toxicity".

In May 1988, at a meeting of the American Society of Clinical Oncology in New Orleans, Dr. Christine Cripps described the results of a Phase II study of lonidamine and radiotherapy for advanced squamous cell cancers of the head and neck.

In November 1988, at a meeting of the InterAmerica Society of Chemotherapy in Buenos Aires, Argentina, Dr. Shailendra Verma spoke on high-dose epirubicin for breast cancer and described other studies using high-dose epirubicin.

At several meetings, Dr. Libni Eapen presented the results of a highly successful trial of concurrent intra-arterial cisplatinum and radiation in locally advanced bladder cancer. In October 1988, he spoke to the American Society of Therapeutic Radiology and Oncology in New Orleans and to meetings in Montreal, New York and Boston.

In September 1988, Dr. Bernd Esche spoke at the European Society of Therapeutic Radiation Oncology in Den Haag on "Carcinoma of the Cervix: Treatment Complications in the Fletcher System". At the same meeting Dr. Juanita Crook described her experience with radiation therapy for carcinomas of the skin, of the nose and nasal vestibule.

Dr. Laval Grimard spoke twice at this same meeting on brachytherapy techniques for carcinomas of the tongue and floor of the mouth.

In March 1989, Dr. Cyril Danjoux attended the annual meeting of the North American Hyperthermia Group in Washington to describe the correlation between hypersensitivity in vitro to ionizing radiation and the adverse reaction to radiotherapy in cancer patients, and lymphoblastic radiosensitivity in cancer patients. In addition, he presented a paper to the Societe Francophone de Cancerologie in Martinique on "Cancer de la Prostate – Traitement par Radiotherapie".

The career scientist program is now solidly established at the Ottawa Centre. All three scientists, Drs. H.C. Birnboim, R.G. Hawley and R.G. Liteplo, carry out research projects supported by grants from the National Cancer Institute of Canada. In addition, Dr. Birnboim has a grant from the Medical Research Council of Canada to study the role of active oxygen species and DNA strand breaks in tumor development. Members of the career scientist group made 13 presentations to national and international meetings in addition to numerous local lectures. During the past year, much has been done to enhance the interaction between members of the University of Ottawa basic research community, the OCTRF career scientists, the Ottawa Regional Cancer Centre's physics research group and the clinical research staff.

Other Centre staff have won grants-in-aid during the past year. Annette O'Connor, R.N., Ph.D., of the University of Ottawa was awarded the 1988 Oncology Nursing Foundation/Bristol Myers Oncology Research Division Grant. With co-investigators, Dr. W.K. Evans, Mrs. C. MacMillan, Ms. S. Joanisse and Ms. C. Dolberg, she will investigate why cancer patients on potentially curative chemotherapy protocols decide not to comply with recommendations for treatment.

Dr. Danielle Perrault received a further NSABP grant to continue the Centre's involvement in the clinical research protocols of this multicentre group.

Dr. Diane Logan has received grants to continue her studies of platelet-derived growth factor and the characterization of cell lines of Kaposi's sarcoma. Also, under the National Health Research and Development Program, she will receive funding for three years from Health and Welfare Canada for the project "Kaposi's Sarcoma – In Vitro Study".

Dr. G.P. Raaphorst and members of the physics department have received NCIC, NSERC, NRC and industry grants for a variety of research projects related to hyperthermia, tumor-cell resistance to radiation and chemotherapy and the development of dynamic radiotherapy. In addition, the physics group has an impressive list of accomplishments that have improved the delivery of radiation and imaging at the Centre.

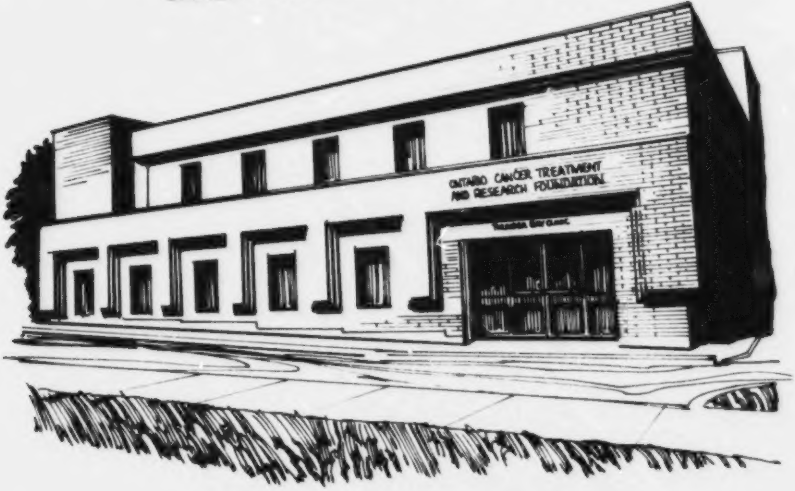
At present, the Centre is bracing itself to accommodate an increased number of cancer patients from the Sudbury and Toronto areas because of a shortage of radiation machines and staff at the Princess Margaret Hospital in Toronto. The Ottawa Centre is able to undertake this added workload only through the dedication of its staff and its commitment to excellent patient care.

Although this report has singled out many individuals for specific achievements during the past year, I wish to thank the entire staff who, working together, created the team that makes it possible to deliver excellent patient care, maintain excellence in teaching and productivity in the research.

W.K. Evans, M.D., F.R.C.P.(C)
Chief Executive Officer

THUNDER BAY REGIONAL CANCER CENTRE

GENERAL HOSPITAL OF PORT ARTHUR


ONTARIO CANCER TREATMENT
AND RESEARCH FOUNDATION
THUNDER BAY CLINIC

Chief Executive Officer:
J.F. Kotalik, M.D.

Radiation Oncologists:
S. Gulavita, M.B., B.S.
M. McLean, M.B., B.Ch.

Medical Oncologist:
H.S. Dhaliwal, M.D.
H.L. Rayner, M.D.

Clinical Assistant:
L. Pratt, M.D.

Physicists:
M. Al-Ghazi, Ph.D.
B. Arjune, M.Sc.
J. Thekkumthala, Ph.D.

Clinical Psychologist:
S. Sellick, Ph.D.

Business Manager:
M.M. Ryan

Nurse Administrator:
L. Bright, Reg.N.

Radiation Therapy Manager:
J.V. Morgan, R.T.

Clinical Trials Manager:
E. Rayner, R.N.

Health Information Services Manager:
M. Kelly, C.C.H.R.A.(C)

Amethyst Lodge Supervisor:
M. Magnusson

At our Centre, the year 1989 has been marked by a steady growth in service, research and education programs. Besides the usual increase in cancer patients, we have had a further increase due to a demand for hematological consultation. Because Northwestern Ontario has no hematologists, and because many physicians know of Dr. Harry Rayner's skill in this area, we are receiving a large number of patients with hematological non-malignant conditions for consultation. While our Centres are not funded for this type of service, we cannot turn these patients away. In the second one-half of the year, during the extreme shortage of radiotherapy services in Southern Ontario, we agreed to accept patients from our radiotherapy referral centre in Toronto. In the last quarter, we treated up to 10 new patients per week, some from Northern Ontario, others from Toronto; normally they would have sought care "down South". Even after these special referrals are discontinued, we expect to receive patients from a much wider area of Northern Ontario because physicians and patients have discovered that our Centre offers good service without waiting. These new patients represent additional work for our staff, however we have enlisted two additional radiotherapy technologists to ease the burden.

Dr. Matthew Al-Ghazi has been promoted to Head of the Department of Medical Physics. Carol Alexson, Manager of Health Information Services, has resigned to accept a position in Southern Ontario, but we have been fortunate to enlist Mrs. Marie Kelly as the new manager. Mrs. Kelly has extensive experience in managing health record departments in general hospitals. Dr. J.A. Chalykoff, our clinical associate in palliative care, has left the Centre to enter private practice, but she will continue to serve in the palliative care on a part-time basis.

We have received permission to hire an administrator and, as this report goes to the printer, candidates are being interviewed. The new administrator's first task will be to initiate the process of renovation and expansion in our Centre. The Foundation has approved and the Ministry of Health has promised to fund the relocation of the greater part of our administrative functions into the basement of our lodge, Amethyst House; this new unit would be connected by a tunnel to the main building. We now face a critical shortage of space in the Centre, particularly with the recent increase in workloads and only scrupulous attention to scheduling permits us to carry on. We hope that the renovated space will be available before the end of 1990.

Our Centre is further handicapped because the host hospital has no assigned oncology beds. As a temporary measure, we arranged with them that chemotherapy patients and critical-care oncology patients will be sent to the same general medical ward rather than being scattered throughout the hospital. When oncology patients are centralized, we can offer better medical supervision, better nursing care and better nurse training.

We continue to serve the community cancer clinics in six outlying towns; in the past year, our oncologists spent more than 50 days away from the Centre to provide this service. In addition, Atikokan has now asked for one of these clinics.

On the research side, we are happy to report an increasing recruitment of patients into clinical trials. Also, progress has been steady in medical physics research, especially in studies of dosimetry of high-energy photons and neutrons. Dr. Sellick, through his appointment at Lakehead University Department of Psychology, has involved several graduate students in projects, which resulted in conference presentations and papers. Some of these are pilot studies, which may develop into larger prospective studies in the psychosocial aspects of cancer.

This year we completed a case-control study of cervical cytology and reported it at Oncology Rounds at McMaster University in Hamilton, in Thunder Bay and at the National Consensus Conference on Cervical Cytology Screening. These provide an important baseline against which to measure subsequent improvement in the prevention of invasive cancer of the cervix. This study was made possible by close co-operation between our Centre, the Foundation's Division of Epidemiology and Statistics, and Dr. N.G. Escott, pathologist at our host hopsital.

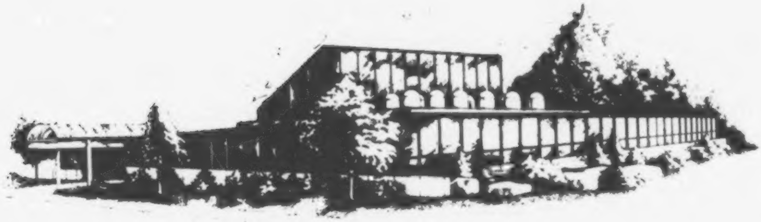
As a result of our academic affiliation with McMaster University and with the continuous co-operation of our colleagues in radiation oncology in Hamilton, we are moving toward rotation of their radiotherapy residents through our Centre. Our first resident arrived in November 1989. In public education, we co-operated last spring with the local Unit of the Canadian Cancer Society to present a public information night on cancer. The success of this venture convinced us that we needed a longer and more highly structured program. As a result, Dr. Dhaliwal organized a full lecture series on cancer diagnosis, prevention and treatment at Lakehead University. Most of our medical staff participated in this series, which was well attended.

These and other accomplishments encourage us to enter the new year with renewed vigor and optimism. We propose to expand our programs further and to continue to perform as a comprehensive cancer centre.

J.F. Kotalik, M.D., D.M.R.T., F.R.C.P.(C)
Chief Executive Officer

TORONTO-BAYVIEW REGIONAL CANCER CENTRE

SUNNYBROOK MEDICAL CENTRE



Chief Executive Officer:
R.D.T. Jenkin, M.B., B.S.

Radiation Oncologists:
I. Ackerman, M.D.
J.M. Balogh, M.D.
M.P. Berry, M.B., B.S.
P.A. Catton, M.D.
P. Davey, M.B., Ch.B.
A.J. Dembo, M.D.
M.A. Doherty, M.B., B.S.
R.G. MacKenzie, M.D.
N.D. Mountifield, M.D.
G.M. Thomas, M.D.
C.S. Young, M.D.

Medical Oncologists:
N.L. Berinstein, M.D.
G. Bjarnason, M.D.
R.A.A. Buckman, M.B., B.Ch.
N.A. Iscoe, M.D.
I.J. Kerr, M.D.
N. Lassam, M.D.
K.I. Pritchard, M.D.
C.A. Sawka, M.D.
D.J.A. Sutherland, M.D.

Clinical Assistants:
P.L. Chart, M.D.
H.M. Kocandrle, M.D.
J.M. Wall, M.D.

Physicists:
G. Doswell,
H.B. Michaels, Ph.D.
P.F. O'Brien, M.Sc.
R.A. Siwek, Ph.D.
M. Woo, Ph.D.

Administrator:
H.B. Wodinsky, M.H.Sc.

Assistant Administrator:
N. Lowe, M.H.Sc.

Administrative Assistant:
K.A. Nicholson

Finance Manager:
B. Copeland

Nurse Administrator:
L.J. Thompson, M.Sc.N.

Chief Radiotherapy Technologist:
S.V. Scott, A.C.(T), R.T.R.

Manager of Health Records:
M. Mistruzzi, C.C.H.R.A.(C)

The year 1989 was something of a roller coaster ride at the Toronto-Bayview Regional Cancer Centre (T-BRCC). On the positive side, we completed the basement renovation, which included two simulators and a planning suite for the Division of Radiation Oncology, a new office suite and an office and conference room area for patient support services (psychology, social work and pastoral care) and the School of Radiation Technology. This renovation had a domino effect, which made necessary major changes in our first floor radiation treatment area, in particular we had to create a new mould room suite in the space previously occupied by our first simulator. The lecture theatre has been relocated and new offices have been created for the nursing division; this allowed us to create two more patient examining room in the ambulatory-care area. The ambulatory care chemotherapy suite has been expanded and the pump program relocated. Because there was no room for a new 6 MeV accelerator, the "footprint" of the building was extended to the south and the bunker for that machine is being constructed, although the machine will not be operational until mid-1990. This last construction represents the first phase of our planned major expansion, which still awaits Ministry approval.

Sunnybrook research tower, adjacent to the T-BRCC, is under construction and should be completed and occupied in mid-1990. At that time, a joint T-BRCC/Sunnybrook Medical Centre (SMC) cancer research program will be initiated. A search is underway for a head for the joint division of cancer research. During the year Dr. Mark Henkelman was appointed Vice-President of Research at SMC; in the near future he will move from PMH with his group of imaging researchers.

The down-side of 1989 was that, at the last moment, plans to merge SMC and the Wellesley Hospital collapsed and, late in the year, there was a crisis in radiation oncology, which was precipitated by a severe shortage of radiation technologists. Thus, at year's end, we were forced to transfer many patients, who require radiation treatment, to our colleagues in Ottawa, Kingston and Thunder Bay. We are indebted to the staff at these centres who have made that extra effort to keep this program going. In the new year we expect to start sending patients to U.S. centres. Even with these unusual arrangements and the hard work of our own staffs, our waiting lists for radiation treatment remain unconscionable.

The Ministry of Health has given Harold Wodinsky, our administrator, a mandate to mount an international recruiting campaign for radiation technologists; hopefully these recruits will provide the interim solution to this province-wide problem. As a long-term solution at the T-BRCC, we plan to expand the School of Radiation Technology next year. The shortage of radiation technologists drew attention to a radiation treatment resource which, in Metropolitan

Toronto, is in trouble. Waiting lists will not be reasonable and we will not have quality radiation treatment in this region until we have a major expansion of the total radiation treatment resource. Until this comprehensive expansion is completed, the T-BRCC will have to refer a proportion of its patientload elsewhere. Thus 1989 has ended on a note of crisis. For the first time since the creation of a province-wide radiation oncology resource more than 40 years ago, we are demonstrably unable to provide this vital service in convenient, timely and appropriate fashion for all cancer patients in the province.

R.D.T. Jenkin, M.B., B.S.
Chief Executive Officer

WINDSOR REGIONAL CANCER CENTRE

METROPOLITAN GENERAL HOSPITAL

Chief Executive Officer:
G.C.K. Mok, M.D.

Radiation Oncologists:
J.A. Gilchrist, M.B., B.S.
L.F. Paszat, M.D.
C.D. Springer, M.B., B.S.

Medical Oncologists:
H.T. Abu-Zahra, M.B., B.Ch.
Z.Y. Alam, M.B., B.S.
D.A. Sicheri, M.D.
S. Yoshida, M.D.

Physicists:
M. Gribble, M.Sc.,
D. Smocovitis, M.Sc.

Business Manager:
E. Hancock

Manager, Radiation Therapy:
M. Rice, A.C. (T)

Head Nurses:
R.A. Girard, Reg. N.
S. Vickers, Reg. N.

Manager of Health Records:
R. Van Der Borgh

In spite of the steady annual increase of new cases, the Windsor Centre had no increase in the numbers of clinical staff in 1989. The only new addition is a dosimetrist, Steve Vasiliadis, who joined our physics department in November 1989.

With the addition of the SL25 linear accelerator, it soon became evident that the AECL's TP11 treatment planning computer was inadequate to meet the demand for daily treatment planning. In March 1989 it was replaced by a newer model, the Theraplan L400 manufactured by Theratronics International. Our present Picker simulator has served us well for the past 14 years but the wear and tear of these years has made it inaccurate and its images poor. We are looking forward to the delivery of a new Toshiba simulator in the spring of 1990. Our physics team did extensive research on several machines by different manufacturers. A team consisting of a physicist, a radiation oncologist, the manager of radiation therapy technologists and a radiation technologist from the simulator room have made several on-site visits to gain "hands-on" experience.

In August, the Centre received verbal approval from the Ministry of Health for an interim renovation to increase the total floor space of our Centre. In a major portion of this renovation, the first floor of the Kildare Wing – a vacant nurses residence belonging to our host hospital – will be linked to our Centre by a covered skywalk. Since it was not built for clinical service, the new floor will be occupied by our Business Office, Health Records Department, Information Services, Clinical Trials Protocol Office and a new library and meeting room. The space gained from this move will be taken up by the Departments of Physics and Radiation Therapy Technology. Two of the four existing examination rooms will be converted to house the new simulator; new examination rooms will be constructed in the current Health Records area. This renovation will meet current need for space, however, judging by our Centre's present rate of growth, we will face another critical shortage of space in three to five years.

Recently we met with the Dean of the Faculty of Science and his senior staff of the University of Windsor to discuss co-operative programs in psychosocial and "wet lab" cancer research. Also we are looking into teaching programs for their nursing school. Symposia are also being planned.

In mid-year, the Essex District Office of the Canadian Cancer Society appointed a new District Director, Miss Brenda McConnell and, more recently, a new Assistant District Director, Mr. Michael Clark. We are forming a liaison committee between the Canadian Cancer Society and the Windsor Regional Cancer Centre. At least four of our oncologists attend meetings in the District and Unit Offices of the Society in the capacity of medical advisors. Dr. Jim Gilchrist has been particularly active with the Riverside Unit, giving talks and helping the Unit to put up posters in the area's shopping malls to promote the programs of the Canadian Cancer Society. Dr. Abu-Zahra serves as medical advisor to the Hospice of Windsor.

This past summer we had one Ivan Smith Fellow, Miss Michelle Pearce – a medical student from Queen's University. While Michelle was here she undertook a project entitled "Measuring Quality of Life in Lung Cancer Patients".

Our new Radiation Technologist School is going well under the direction of Ms. Margaret Rice and Mrs. Gail McBrayne. This fall we took in a third student and look forward to the first graduating class in the summer of 1990.

G.K. Mok, M.D
Chief Executive Officer

SERVICE LOAD

The following tables describe the service load of the Foundation's seven regional cancer centres and the Northeastern Ontario Oncology Program in Sudbury during the calendar year 1988.

In 1988, 55,248 patients were seen at these centres. Of these, 92% had malignant lesions and, of these lesions, 16,853 were new to the centres (Table I). Of cases referred for non-malignant conditions, 80% were first seen in 1988 (Table II). The majority of the non-malignant conditions were seen for follow-up and consultation (1,439 and 652 respectively). In all, 11,559 malignant cancer cases were treated by radiotherapy (Table III); of these, 5,481 were treated by cobalt units, 5,192 by a linear accelerator, and 886 by other methods of radiotherapy.

During the year, patients made 572,529 visits to the regional cancer centres and the Northeastern Ontario Oncology Program, and the majority, 558,919, were for treatment of malignant disease (Table IV). Of all radiation treatments, 89% were given on an outpatient basis (Table V).

As of January 1, 1982, with the implementation of the Patient Care Management System (PCMS) in the centres, it has been possible to retrieve data in more detail than was possible in previous years. The current tabulations are taken from data as of August 1989. Consultation and follow-up visits have been divided and appear in separate columns in Tables I, II and IV. Simulations are shown in Table V but are not included in the totals. It must be emphasized that these tables are comparable only with the service load tables published for 1982 to 1987 inclusive; they are not comparable with those for the years before PCMS was implemented.

TABLE I

Malignant Caseload During 1988*

TREATMENT CENTRE	TREATED				CONSULTATION ONLY	FOLLOW-UP ONLY	TOTAL
	Radiation	Radiation and Chemotherapy	Chemotherapy	Procedures			
	Cases New in Current Year						
Hamilton	1,126	296	668	25	590	898	3,603
Kingston	436	101	137	17	194	292	1,177
London	971	298	438	75	566	769	3,117
Ottawa	1,053	281	550	142	414	736	3,176
Sudbury	-	-	259	6	124	135	524
Thunder Bay	192	47	100	4	77	126	546
Toronto-Bayview	1,261	243	303	384	587	796	3,574
Windsor	379	90	212	30	140	285	1,136
TOTAL	5,418	1,356	2,667	683	2,692	4,037	16,853
	Cases Registered in any Previous Year						
Hamilton	511	264	1,092	58	162	5,519	7,606
Kingston	186	89	298	32	122	2,491	3,218
London	365	222	643	200	203	4,506	6,139
Ottawa	360	396	1,087	149	125	6,265	8,382
Sudbury	-	-	252	8	3	230	493
Thunder Bay	72	49	169	12	39	1,089	1,430
Toronto-Bayview	321	169	338	137	87	2,751	3,803
Windsor	110	106	422	58	65	2,325	3,086
TOTAL	1,925	1,295	4,301	654	806	25,176	34,157
TOTAL ALL MALIGNANT	7,343	2,651	6,968	869	1,000	29,213	51,010

*Includes cases seen at peripheral clinics.

TABLE II

Other (Non-Malignant) Caseload During 1988*

TREATMENT CENTRE	TREATED				CONSULTATION ONLY	FOLLOW-UP ONLY	TOTAL
	Radiation	Radiation and Chemotherapy	Chemotherapy	Procedures			
	Cases New in Current Year						
Hamilton	50	-	39	17	93	237	436
Kingston	7	-	58	95	185	304	649
London	33	2	38	378	74	206	731
Ottawa	26	1	7	170	21	96	321
Sudbury	-	-	2	-	9	10	21
Thunder Bay	-	-	1	10	45	68	124
Toronto-Bayview	13	-	5	255	163	322	758
Windsor	5	2	16	52	62	196	333
TOTAL	134	5	166	977	652	1439	3373
	Cases Registered in any Previous Year						
Hamilton	3	-	-	-	1	35	39
Kingston	1	-	3	-	1	27	32
London	1	-	2	1	3	46	53
Ottawa	3	-	2	22	-	83	110
Sudbury	-	-	-	-	-	-	-
Thunder Bay	-	-	-	-	-	13	13
Toronto-Bayview	1	-	-	72	8	495	576
Windsor	-	-	3	-	-	39	42
TOTAL	9	-	10	95	13	738	865
TOTAL ALL MALIGNANT	143	5	176	1072	665	2177	4238

*Includes cases seen at peripheral clinics.

TABLE III

Cases Treated During 1988 by Method of Radiotherapy

METHOD OF TREATMENT	HAMILTON	KINGSTON	LONDON	OTTAWA	THUNDER BAY	TORONTO BAYVIEW	WINDSOR	TOTAL
	Malignant Neoplasms							
Superficial x-ray	140	172	28	19	23	54	83	519
Deep x-ray	1	-	-	-	-	-	-	1
Cobalt^{60}	1,453	377	617	1,344	150	1,084	456	5,481
Cesium^{137}	-	-	-	-	-	-	-	-
Betatron	-	-	-	-	-	-	-	-
Linear accelerator	783	351	1,602	972	223	1,066	195	5,192
Intracavitary	72	17	81	35	5	51	15	276
Interstitial	10	2	14	53	1	8	-	88
Moulds and applicators	-	-	2	-	-	-	-	2
Systemic isotopes	-	-	-	-	-	-	-	-
Others*	-	-	-	-	-	-	-	-
SUB-TOTAL	2,459	919	2,344	2,423	402	2,263	749	11,559
Simulations	2,936	942	2,826	3,270	418	2,596	1,559	14,547
	Other Non-Malignant							
Superficial x-ray	1	-	-	1	-	-	-	2
Deep x-ray	-	-	-	-	-	-	-	-
Cobalt^{60}	27	2	11	22	-	8	5	75
Cesium^{137}	-	-	-	-	-	-	-	-
Betatron	-	-	-	-	-	-	-	-
Linear accelerator	26	6	8	8	-	5	2	55
Intracavitary	-	-	-	-	-	-	-	-
Interstitial	-	-	17	-	-	-	-	17
Moulds and applicators	-	-	-	-	-	-	-	-
Systemic isotopes	-	-	-	-	-	-	-	-
Others*	-	-	-	-	-	-	-	-
SUB-TOTAL	54	8	36	31	-	13	7	149
Simulations	70	12	26	36	-	17	9	170
TOTAL**	2,513	927	2,380	2,454	402	2,276	756	11,708

* Others include radiation codes unknown.
** A case can be treated by more than one method per year. Simulations are displayed but are not included in the totals.

TABLE IV

Service Load, 1988

TREATMENT CENTRE	VISITS FOR						TOTAL VISITS
	Treatment			Non-Treatment			
	Radiation	Chemotherapy	Procedures	Simulations	*Consultations	Follow-up Visits	
	Visits for Malignant Neoplasms						
Hamilton	32,160	16,756	421	2,936	5,976	38,978	97,227
Kingston	12,167	4,316	976	942	2,173	24,235	44,809
London	32,838	8,913	1,479	2,826	4,904	39,978	90,938
Ottawa	39,239	18,793	1,553	3,270	6,075	72,961	141,891
Sudbury	-	6,522	612	-	544	16,524	24,202
Thunder Bay	6,874	2,970	524	418	1,038	9,542	21,366
Toronto-Bayview	32,446	4,944	1,514	2,596	4,778	38,882	85,160
Windsor	12,774	6,977	871	1,559	1,660	29,485	53,326
TOTAL	168,498	70,191	7,950	14,547	27,148	270,585	558,919
	Other Non-Malignant						
Hamilton	631	107	48	70	277	652	1,785
Kingston	127	159	416	12	441	1,638	2,793
London	188	106	759	26	286	1,024	2,389
Ottawa	295	113	352	36	158	676	1,630
Sudbury	-	13	3	-	14	65	95
Thunder Bay	-	2	54	-	113	346	515
Toronto-Bayview	190	10	406	17	738	1,383	2,744
Windsor	59	74	161	9	289	1,067	1,659
TOTAL	1,490	584	2,199	170	2,316	6,851	13,610
TOTAL ALL VISITS	169,988	70,775	10,149	14,717	29,464	277,436	572,529

* Consultations includes re-consultations.

TABLE V

Treatments by Radiotherapy During 1988, In-Patients and Out-Patients

METHOD OF TREATMENT	HAMILTON		KINGSTON		LONDON		OTTAWA		THUNDER BAY		TORONTO BAYVIEW		WINDSOR		TOTAL	
	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out
Malignant Neoplasms																
Superficial x-ray	9	706	11	1,231	4	185	-	157	-	187	1	431	17	867	42	3,764
Deep x-ray	-	10	-	-	-	-	-	-	-	-	-	-	-	-	-	10
Cobalt^{60}	1,361	15,951	720	5,179	1,944	4,965	2,921	16,353	605	2,049	1,687	10,412	1,140	6,451	10,378	61,360
Cesium^{137}	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Betatron	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Linear accelerator	666	13,371	482	4,522	3,157	22,476	1,743	14,919	425	3,554	1,160	18,685	164	4,118	7,797	81,645
Intracavitary	76	-	20	-	91	-	38	-	5	-	51	-	17	-	298	-
Interstitial	10	-	2	-	2	12	55	-	1	-	8	-	-	-	78	12
Moulds and applicators	-	-	-	-	2	-	-	-	-	-	-	-	-	-	2	-
Systemic isotopes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Others*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SUB-TOTAL	2,122	30,038	1,235	10,932	5,200	27,638	4,757	31,429	1,036	5,790	2,907	29,528	1,338	11,436	18,595	146,791
Simulations	341	2,595	161	781	643	2,183	615	2,655	100	318	303	2,293	175	1,384	2,338	12,209
Other Non-Malignant																
Superficial x-ray	-	1	-	-	-	-	-	11	-	-	-	-	-	-	-	12
Deep x-ray	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cobalt^{60}	-	210	-	19	-	48	3	143	-	-	-	25	-	53	3	498
Cesium^{137}	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Betatron	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Linear accelerator	12	408	32	76	15	106	-	119	-	-	4	161	-	6	63	876
Intracavitary	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Interstitial	-	-	-	-	-	19	-	-	-	-	-	-	-	-	-	19
Moulds and applicators	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Systemic isotopes	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Others*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SUB-TOTAL	12	619	32	95	15	173	3	273	0	0	4	186	-	59	66	1,405
Simulations	1	69	7	5	1	25	1	35	-	-	-	17	-	9	10	160
TOTAL OF ALL TREATMENTS	2,134	30,657	1,267	11,027	5,215	27,811	4,760	31,702	1,036	5,790	2,911	29,714	1,338	11,495	18,661	148,196

*Others include radiation codes unknown.

CONSULTATIVE AND FOLLOW-UP CLINICS

The distribution of these clinics reflects the general zones of service of the Foundation's Regional Cancer Centres in Hamilton, Kingston, London, Ottawa, and Thunder Bay; and of the Princess Margaret Hospital, Toronto.

HAMILTON	
Brantford	St. Joseph's Hospital
Burlington	Joseph Brant Memorial Hospital
Cambridge (Galt)	Cambridge Memorial Hospital
Guelph	Guelph General Hospital
Hamilton	McMaster Medical Centre and St. Joseph's Hospital
Niagara Falls	Greater Niagara General Hospital
St. Catharines	Hotel Dieu Hospital
Welland	Welland County General Hospital
KINGSTON	
Trenton	Trenton Memorial Hospital
LONDON	
Chatham	Public General Hospital
Kitchener	Kitchener-Waterloo Hospital
London	St. Joseph's Health Centre
Owen Sound	Grey-Bruce Regional Health Centre
Sarnia	St. Joseph's Hospital and Sarnia General Hospital
St. Thomas	St. Thomas-Elgin Hospital
Stratford	Stratford General Hospital
Wingham	Wingham and District Hospital
Woodstock	Woodstock General Hospital
OTTAWA	
Cornwall	Cornwall General Hospital and Hotel Dieu Hospital
Ottawa	Riverside Hospital, Montfort Hospital and Queensway-Carleton Hospital
Pembroke	Pembroke Civic Hospital
THUNDER BAY	
Dryden	Dryden District General Hospital
Fort Frances	La Verendrye General Hospital
Geraldton	Geraldton District Hospital
Hearst	Notre-Dame Hospital
Sioux Lookout	Sioux Lookout General Hospital
Terrace Bay	The McCausland Hospital

TORONTO

North Bay	North Bay Civic Hospital
Peterborough	St. Joseph's Hospital
Sault Ste. Marie	Plummer Memorial Public Hospital
Sudbury	Laurentian Hospital
Timmins	St. Mary's Hospital

CLINICAL CONSULTANTS AT THE OCTRF REGIONAL CANCER CENTRES AND THE PRINCESS MARGARET HOSPITAL

(As at December 31, 1989)

OCF Hamilton Centre:

M. Ali, M.D.
S. Archibald, M.D.
H.W. Beattie, M.D.
A.M. Benger, M.D.
W.F. Bennett, M.D.
I.W. Blackstone, M.D.
M. Brain, M.D.
A.J. Campbell-Moscrop, M.D.
B. Clark, M.D.
D. Clark, M.D.
J. Collins, M.D.
I.R. Davis, M.D.
P.B. Dent, M.D.
R. deVilliers, M.D.
B. Findlay, M.D.
J.D. Gowing, M.B., B.S.
R.A. Hadden, M.D.
J. Harvey, M.D.
D.A. Hitch, M.D.
B.S. Jackson, M.D.
P. Jenkin, M.D.
J. Kearns, M.D.
P. Knight, M.B., Ch.B.
J.A. McBride, M.B., Ch.B.
R. Meyer, M.D.
W. Nicholson, M.D.
S.E. O'Brien, M.D.
W.L. Orovan, M.D.
M. Rathbone, M.D.
W.D. Rider, M.B., Ch.B.
J.T. Roberts, M.B., Ch.B.
D. Rosenthal, M.D.
M. Samosh M.D.
D. Sauder, M.D.
D. Savelli, M.D.
B. Trossman, M.D.
P. Vasarinsh, M.D.
I. Walker, M.D.
J. Weitz, M.D.
W.E.C. Wilson, M.D.
C. Woolever, M.D.
J.E.M. Young, M.D.

OCF Kingston Centre:

J.M. Blakeman, M.D.
H. Brown, M.D.
S.C.P. Bryson, M.D.
J.A. Carmichael, M.D.
W.E.N. Corbett, M.D.
D. Dexter, M.D.
B.E. Elliott, Ph.D.
H.B. Dinsdale, M.D.
S.F. Hall, M.D.
J.W. Kerr, M.D.
K.W. Mackie, M.D.
D. McIntosh, M.D.
R.J. Riopelle, M.D.
D.M. Robertson, M.D.
M. Silva, M.D.
H.D. Steele, M.D.
E.E. Sterns, M.D.
K. Taguchi, M.D.
D.M.L. Williams, M.D.

OCF London Centre:

H.H. Allen, M.D.
W.B. Barton, M.D.
R.M. Barr, M.D.
U. Bite, M.D.
A.E. Cairney, M.D.
M. Carey, M.D.
J. Chertkow, M.D.

J. Chin, M.D.
J. Coles, M.D.
R.F. Del Maestro, M.D.
G. DeRose, M.D.
L.L. deVeber, M.D.
A.A. Driedger, M.D.
J. Duff, M.D.
D. Girvan, M.D.
J. Gonder, M.D.
R.W. Gottschalk, M.D.
L.C. Guenther, M.D.
J. Harris, D.D.S.
H. Heeneman, M.D.
R.L. Holliday, M.D.
R. Inculet, M.D.
M.J. Inwood, M.D.
M.E. Kirk, M.D.
H.Lampe, M.D.
D. Macdonald, M.D.
J.A. McCredie, M.D.
R.M. McFarlane, M.D.
T.D. McLarty, M.D.
I.R. McWhinney, M.D.
E. Meads, M.D.
D.B. Meltzer, M.D.
D. Moulin, M.D.
J. Nisker, M.D.
J.F. Sangster, M.D.
I.D.F. Schofield, D.D.S.
R. Shearer, M.D.
M. Smout, M.D.
W.K. Stavraky, M.D.
R. Thomas, M.D.
D.M. Wexler, M.D.
J. Wyatt, M.D.

OCF Ottawa Centre:

G.Allen, M.D.
J.W. Atkinson, M.D.
L.I. Avruch, M.D.
M.G. Bard, M.D.
P.T. Barron, M.B., Ch.B.
A.W. Barry, M.D.
A. Baxter, M.B., B.S.
P. Beaudry, M.D.
R. Belanger, M.D.
D.N. Bell, M.D.
M. Bell, M.D.
P. Benoit, M.D.
J.M. Benzie, M.D.
J.M. Beresford, M.B., Ch.B.
M. Bertrand, M.D.
J. Bormanis, M.D.
A.G. Bouchard, M.D.
L. Busque, M.D.
L.J. Byford, M.D.
G.E. Catton, M.B., B.S.
S. Chater, M.D.
C.K. Chew, M.D.
J.C. Clark, M.D.
J.M. Cowan, M.B., Ch.B.
J. Cox, M.D.
A. Crepeau, M.D.
M. Curran, M.D.
V. Da Silva, M.D.
Y. de la Bastide, L.R.C.P. (U.K.)
J.J. Deneault, M.D.
J.E. Devitt, M.D.
J. Drouin, M.D.
M.J. Duncan, M.D.
L. Eidus, M.D.
R. Elliott, M.D.
R.J. Fairfull-Smith, M.B., Ch.B.
J.B. Freeman, M.D.
G. French, M.D.
N.G. Futter, M.D.
G. Garber, M.D.
L. Garnett, M.D.
S. Garniss-Jones, M.D.
E. Gear, M.D.
J. Gerin-Lajoie, M.D.
A. Giachino, M.D.
L. Lu-Godbout, M.D.
Z. Grahovac, M.D.
J.E. Green, M.D.
P. Hamilton, M.D.

D.I. Hammond, M.D.
A. Haq, M.D.
J. Hardie, B.D.S.
M. Hardy, M.D.
R. Heringer, M.D.
D.P. Hill, M.D.
R.B. Hladkowicz, M.D.
R.V. Hodder, M.D.
E. Hsu, M.D.
L.B. Huebsch, M.D.
H. Hugenholtz, M.D.
J.B. Hurtig, M.D.
A.H. Irvine, M.D.
R. Jackson, M.D.
C. Jensen, M.D.
T.G. Jones, M.B., B.S.
B. Kirk, M.D.
J. Kitts, D.D.S.
G. Laframboise, M.D.
A. Lamothe, M.D.
B.M. Lefebvre, M.D.
G.N. Lewis, M.D.
B. Luke, M.D.
P.C. MacEwen, M.D.
J.P. MacLeod, M.D.
K.T. Mai, M.D.
S. Markman, M.D.
R. Martineau, M.D.
N. Mayer, M.D.
R.W. McIntyre, M.D.
W.A. McLeish, M.D.
J. McKenna, M.D.
S. Meban, M.B., Ch.B.
S. Mercer, M.D.
N.A. Mikhael, M.D.
D. Miller, M.D.
G. Mintsioulis, M.D.
V. Monpetit, M.D.
D. Moors, M.D.
J.P. Murnaghan, M.D.
N.J. Nathan, M.D.
M. Navarro, M.D.
R. Nelson, M.D.
K. Nolan, M.D.
P.F. Odell, M.D.
B. Olberg, M.D.
D.J. O'Neil, M.D.
M. Orizaga, M.D.
A. Peloquin, M.D.
J.P. Penning, M.D.
E.L. Perez, M.D.
D.G. Perkins, M.D.
E.W. Peterson, M.D.
R.A. Peterson, M.D.
M. Prefontaine, M.D.
D.N. Preston, M.D.
D.R. Pushman, M.D.
P. Rasuli, M.D.
G. Reid, M.D.
R.H. Reid, M.D.
D. Reid, M.D.
M.T. Richard, M.D.
R.N. Rivington, M.D.
L. Robinson, M.D.
J. Robblee, M.D.
O.P. Rosaeg, M.D.
N.A. Russell, M.D.
H.J. Sachs, M.D.
R. Saginur, M.D.
B. Samson, M.D.
G.J. Sarwer-Foner, M.D.
G. Sauve, M.D.
A.C. Scott, M.D.
J. Seely, M.D.
F.M. Shamji, M.D.
S.Y. Shirley, M.D.
S.S. Silver, M.D.
M. Silverman, M.D.
D.S. Skene, M.D.
G. Skidmore, M.D.
E.E. Spindler, M.D.
H. Tao, M.D.
J.R. Taylor, M.D.
J. Thomas, M.D.
E.N. Thompson, M.D.
F.E. Thompson, M.D.

W.G. Thompson, M.D.
M. Tousignant, M.D.
G.N.W. Tse, M.D.
H.K. Uhthoff, M.D.
F.W. Vaillancourt, M.D.
L.G. Van Wyck, M.D.
C. Vezina, M.D.
P. Walker, M.D.
V. Walley, M.D.
W.G. Walsh, M.D.
H. Warnes, M.D.
C. Watters, M.D.
L. Weatherhead, M.D.
D.S. Whittingham, M.D.
K.B. Wilson, M.D.
R.W. Yarnell, M.D.
H. Yazdi, M.D.

OCF Sudbury - Northeastern Ontario Oncology Program:

J. Abourbih, M.D.
R. Bergh, M.D.
J.M. Dahmer, M.D.
J.F. D'Aloisio, M.D.
G. Helie, M.D.
V. Kumar, M.D.
R. Odhiambo, M.D.
A. Ogundimu, M.D.
L.Q. Wong, M.D.

OCF Toronto-Bayview Centre:

J.D. Anderson, M.D.
D. Assaad, M.D.
R.S. Bell, M.D.
B.D. Birt, M.B., B.S.
G. Bradley, M.D.
P.L. Chan, M.D.
D.H. Cowan, M.D.
G.M. Davies, M.B., B.Ch.
C. De Angenis, Pharm.D.
A.D. DePetrillo, M.D.
M. Fazl, M.D.
J.L. Freeman, M.D.
L. From, M.D.
R. Gilbert, M.D.
J.S. Gruss, M.B., B.Ch.
S. Hanna, M.B., B.Ch.
A.W. Harrison, M.D.
S. Huang, M.D.
J. Hurwitz, M.D.
J.A. Jambrosik, M.D.
N.A. Kerenyi, M.D.
L. Klotz, M.D.
A. Kolin, M.D.
A.J. Lewis, M.D.
J.H.P. Main, D.D.S.
M.A. McKenzie, M.D.
H.A.B. Miller, M.B., B.S.
I. Morova-Protzner, M.D.
B.Y. Ngan, M.D.
R.J. Osborne, M.D.
P.H. Pinkerton, M.D.
J.H. Phillips, M.D.
E.R. Pohlman, M.D., C.M.
P. Poidre, M.D.
B.P. Rosen, M.D.
D.W. Rowed, M.D.
M.L. Schwartz, M.D.
J.L. Semple, M.D.
J.S. Senn, M.D.
P.A. Shaw, M.D.
J.R. Srigley, M.D.
P.K. Shuen, M.D.
S.E. Sutherland, M.D.
G.A. Taylor, M.D.
K. Taylor, Ph.D.
M. Tile, M.D.
M.E. Tweeddale, M.D.
B.C. Walters, M.D.
P.M. Webster, M.D.

The Princess Margaret Hospital, Toronto:

P.W. Alberti, M.B., B.S.
U. Ambus, M.D.
J.D. Anderson, D.D.S.

A.G. Andrews, D.D.S.
A.G. Awad, M.D.
M.A. Baker, M.D.
J.L.M. Bean, M.D.
R.S Bell, M.D.
M. Bernstein, M.D.
N. Bharatwal, M.D.
M.E. Blackstein, M.D.
J.M.A. Bohnen, M.D.
J.B. Boyd, M.D.
T.D.R. Briant, M.D.
A.W. Bruce, M.B., Ch.B.
D.P. Bryce, M.D.
P.S. Bryson, M.D.
C.B. Bubela, M.D.
M.B. Buckspan, M.D.
M. Bulbul, M.D.,
M.L. Bunker, M.D.
J.J. Caesar, M.D.
C.K. Chan, M.D.
H.S.L. Chan, M.B., B.S.
A.W. Chisholm, M.D.
J.G. Connolly, M.D.
D.H. Cowan, M.D.
J.S. Crawford, M.D.
P.L. Darby, M.B., B.S.
A.D. DePetrillo, M.D.
L.G. Douglas, M.D.
I. Dube, Ph.D.
C. Dzerko, M.D.
W.M. Easterbrook, M.D.
R.J. Evans, M.D.
R.E. Falk, M.D.
R.M. Filler, M.D.
E.B. Fish, M.D.
B.K. Fisher, M.D.
J.A. Fisher, M.D.
M.M. Fisher, M.D.
A.E. Franklin, Ph.D.
B.L. Gallie, M.D.
W.O. Geisler, M.D.
A.H. Gerulath, M.D.
R.J. Ginsberg, M.D.
C.M. Godfrey, M.D.
M. Goldberg, M.D.
S.D. Goldberg, M.D.
P. Goodwin, M.D.
D.A. Gordon, M.D.
P. Gullane, M.B., B.Ch.
G. Haber, M.D.
J.A. Hakes, M.B., Ch.B.
M.L. Halperin, M.D.
W.J. Hannah, M.D.
G.D. Hart, M.D.
R.H.A. Haslam, M.D.
D.E. Hastings, M.D.
R.I. Hector, M.D.
C. Hegarty, M.B., B.Ch.
C.H. Hollenberg, M.D.
R. Hopkins, D.D.S.
N.S. Hradsky, M.D.
M.A. Hutcheon, M.D.
R.H. Hyland, M.D.
C.G. Jamieson, M.B., B.S.
R.D.T. Jenkin, M.B., B.S.
S.E. Jelenich, M.D.
M.A. Jewett, M.D.
D.P. Jones, M.D.
A.T. Jousse, M.D.
A.S. Katz, M.D.
M. Kazden, M.D.
A. Keresteci, M.D.
W.K. Kerr, M.D.
D.W. Killinger, M.D.
M.H. King, M.D.
G.H. Knutson, M.D.
B. Langer, M.D.
F. Langer, M.D.
V.G. Lawson, M.D.
K. Lee, M.D.
G.M. Lickrish, M.B., Ch.B.
F.H. Lowy, M.D.
W.J.C. MacArthur, M.D.
R.D. MacDonald, M.D.
I.M. MacKay, M.D.
T.A. MacKenzie, M.D.

L.J. Mahoney, M.D.
J.H.P. Main, D.D.S.
N.E. Marcon, M.D.
J.T. Marotta, M.D.
A.G. Matlow, M.D.
R.J. McBroom, M.D.
D. McCready, M.D.
J.S. McGrail, M.D.
J.W. Meakin, M.D.
W.G. Middleton, M.D.
C.B. Mortimer, M.D.
P.J. Muller, M.D.
J. Murphy, M.D.
T.M. Murray, M.D.
R.A. Mustard, M.D.
R.E. Myers, M.D.
R.J. Osborne, M.D.
F.R. Papsin, M.D.
G.A. Patterson, M.D.
F.G. Pearson, M.D.
R.G. Perrin, M.D.
D.G. Potts, M.D.
K. Psihramis, M.D.
K. Pritchard, M.D.
K.P. Pritzker, M.D.
P. Ramachandran, M.D.
C.A. Ramsay, M.D.
J.T. Rankin, B.M., B.Ch.
B. Rosen, M.D.
I.B. Rosen, M.D.
L. Rotstein, M.D.
J.S. Senn, M.D.
S. Sidlofsky, M.D.
M.D. Silver, M.D.
E.R. Simpson, M.D.
H.S. Smyth, M.D.
H.A. Smythe, M.D.
M.J. Sonley, M.D.
M.L. Soots, M.D.
A.H. Squires, M.D.
R.M. Stone, M.D.
P. Straka, M.B., Ch.B.
D.J. Sutherland, M.D.
J.D. Swales, M.D.
J.M. Symington, B.D.S.
H. Tanzer, M.D.
S.A.P. Tindal, M.B., Ch.B.
J. Trachtenberg, M.D.
M.L.S. Vachon, Ph.D.
R. Volpe, M.D.
C.P.N. Watson, M.D.
N.A. Watters, M.D.
G.D. Webb, M.D.
R.H. Wilkinson, M.D.
C.C. Williams, M.D.
R.E. Wood, D.D.S.
L. Wright, Ph.D.
F.R.H. Wrigley, M.B., B.S.
A. Zipursky, M.D.
R.M. Zuker, M.D.

THE ONTARIO CANCER INSTITUTE

THE ONTARIO CANCER INSTITUTE

incorporating

THE PRINCESS MARGARET HOSPITAL

Dr. D.R. Carlow
President and Chief Executive Officer
500 Sherbourne Street
Toronto, Ontario M4X 1K9
Telephone: (416)924-0671

Medical Oncology:

R.E. Alison, M.D.*
D.E. Bergsagel, M.D.
N.F. Boyd, M.B., B.S.
J.E. Curtis, M.D.
C. Erlichman, M.D.
R. Feld, M.D.
R. Hasselback, M.D., C.M.
J.M. Meharchand, M.B., Ch.B.
H.A. Messner, M.D.
M.D. Minden, M.D.
M. Moore, M.D.
I.C. Quirt, M.D.
J.F.G. Sturgeon, M.B., B.S.
I.F. Tannock, M.D.
D. Warr, M.D.

Radiation Oncology:

R. Bissett, M.D.
R.S. Bush, M.D.
R.M. Clark, M.B., B.S.
B.J. Cummings, M.B., Ch.B.
W. Duncan, M.B., Ch.B.
P.J. Fitzpatrick, M.B., B.S.*
A. Fyles, M.D.
M.K. Gospodarowicz, M.D.
N.V. Hawkins, M.B., B.S.*
T.J. Keane, M.B., B.Ch.
N.J. Laperriere, M.D.
P.D. Lefebvre
W. Levin, M.B., Ch.B.
F.F. Lui, M.D.
B. O'Sullivan, M.B., B.Ch.
D.G. Payne, M.D.
J.F. Pringle, M.B., Ch.B.
G.A. Rawlings, M.D.
W.J. Simpson, M.D.
S.B. Sutcliffe, M.D.
P. Warde, M.B., B.Ch.
S. Wong, M.D.
J.L. Yeoh, M.D.

Dentistry:

W.G. Maxymiw, D.D.S.

Diagnostic Imaging:

R. Blend, M.B., B.S.
R. Goldberg
S. Herman, M.D.
R. Peto, M.D.

Nuclear Medicine:

I. Boxen, M.D.

Pathology:

J.S. Carruthers, M.D.*
V.L. Fornasier, M.D.
V. Jay, M.B., B.S.
G.J. Laroye, M.D.
N. Miller, M.D.
B.J. Patterson, M.D.
M.E. Platts, M.D.*
H. Richmond, M.B., Ch.B.
L.M. Sugar, M.D.*
T. Treger, M.D.

Microbiology:

P.G. Tuffnell, M.D.

Physics :

H. Alasti-Hamed, M.Sc.
M.C. Archer, Ph.D.
M.J. Bronskill, Ph.D.
J.R. Cunningham, Ph.D.*
G. DeBoer, Ph.D.
S. Foster, Ph.D.
D.M. Galbraith, B.Sc.
J. Grant, M.Sc.
R.M. Henkelman, Ph.D.
R.P. Hill, Ph.D.
J W. Hunt, Ph.D.
B. Japp, B.Sc.
J. Jezioranski, M.Sc.
P.M.K. Leung, Ph.D.
M. Lumley, M.Sc.
C. Mah, M.Sc.
A. Mosseri, M.Sc.
F.P. Ottensmeyer, Ph.D.
D. Plewes, Ph.D.

A.M. Rauth, Ph.D.
J.A. Rawlinson, M.Sc.
S. Rose, M.Eng.
D. Spencer, Ph.D.
W.B. Taylor, B.Eng.
J. Van Dyk, M.Sc.
G.F. Whitmore, Ph.D.
M. Yaffe, Ph.D.

Biological Research:

S. Benchimol, Ph.D.
R. Buick, Ph.D.
A.J. Cunningham, Ph.D.
J. Gariepy, Ph.D.
R. Gronostajski, Ph.D.
V. Ling, Ph.D.
H. Llewellyn-Thomas, Ph.D.
T.W. Mak, Ph.D.
E.A. McCulloch, M.D.
R.G. Miller, Ph.D.
S. Minkin, Ph.D.
N. Miyamoto, Ph.D.
C. Paige, Ph.D.
J.E. Till, Ph.D.
D. Tritchler, Ph.D.

*Retired during 1989

Administration:

R. Buick, Ph.D., Vice-President Research
C. Charlton, M.A., Vice-President Resource Development
E. Govoni, Vice-President Finance
A. Headricks, Vice-President Human Resources
J.P. Holder, Vice-President Nursing
J.E. Ratz, Vice-President Planning and Hospital Services
S. B. Sutcliffe, M.D., Vice-President Oncology Programs
T. Warner, Vice-President Quality and Utilization Management
T.J.D. West, Asst. Vice-President Clinical Services
W. Wilkinson, Asst. Vice-President Support Services

Manager of Health Records:

A. Buchanan, B.A., C.C.H.R.A.(C)

Librarian:

C. Morrison, B.A., M.L.S.

We have a unique opportunity to reflect on the achievements of the past 30 years as we move ahead with plans to rebuild on University Avenue. The past year was also one of the most difficult in the history of the organization as we faced critical manpower shortages, particularly in nursing and radiation therapy, and struggled to cope with the impact this had on our ability to care for patients.

In the fall of 1989 our waiting list grew to 300 patients and waiting times to start radiation treatment stretched up to six weeks. However, as with many crisis situations, this critical point yielded unique opportunities. In response to this crisis, we helped to develop a provincial patient referral program which has enabled the OCI/PMH and the OCTRF regional cancer centres to ensure that all patients receive timely treatment despite heavy workloads in the Metropolitan Toronto region. The Ministry of Health has provided program enhancements for radiation therapy, clinical physics, radiation oncology and in psychosocial support. With the OCTRF, we have organized a joint recruitment effort to bring more radiation therapy technologists into the province.

This situation emphasized the need for both – the expansion of provincial radiation facilities, which is underway, and for strong strategic planning for future provincial oncology needs. Therefore we are pleased that the Ministry of Health has endorsed the OCI/PMH-OCTRF proposal for the formation of the Ontario Cancer Control Agency and are confident that, during the coming year, the Ministry of Health will expedite these plans.

Within OCI/PMH, we are challenged to find ways to develop a corporate climate that will foster our tradition of excellence in patient care and innovative research in the face of a rapidly changing and stressful health-care environment. To create a supportive climate, we restructered the corporate management team in the spring. This was the first step in organizing people and programs for effective resource management for the massive planning functions ahead, and for developing future strategies. One of the new positions, Vice-President of Quality and Resource Management, which is the first position at that level in Canada, reflects our focus on total organizational quality. After meeting in several retreats, we have completed a strategic plan, which spells out OCI/PMH's role as a comprehensive cancer centre.

During the past year, staff worked hard to develop a functional program for the new building on University Avenue. We explored new options for shared service arrangements with other hospitals so as to make efficient use of available resources. Zeidler Roberts Partnership developed this program into a creative hospital design that will meet our patients' needs and will preserve two heritage buildings on the site.

We have received another two-year award from the Canadian Council on Health Facilities Accreditation. This award recognizes organizational excellence in the face of inadequate physical facilities, a situation that cannot be resolved until we move into the new hospital.

In the research divisions the scientists in imaging research will have larger facilities and a broader patient base when they move to Sunnybrook Hospital at the end of 1990. This imaging team is one of the top groups in North America and the OCI/PMH will miss them. However the six senior research positions they will vacant, will give us an opportunity to expand our research into new areas.

To guide the development of these research programs, Dr. Ronald Buick, a senior scientist at OCI/PMH for the past 10 years, was appointed to the new position of Vice-President Research.

Also as part of the corporate restructuring, Dr. Simon Sutcliffe, a senior radiation oncologist at OCI/PMH, was appointed to the new position of Vice-President Oncology. Catherine Charlton was also appointed Vice-President Resource Development to support our fundraising programs.

During the year we were saddened when Dr. Peter Fitzpatrick left after 25 years to become Professor and Chairman of the Department of Radiation Oncology at Dalhousie University, Physician-in-Chief at the Cancer Treatment and Research Foundation of Nova Scotia and Director of the Halifax clinic at Victoria General Hospital. Also Drs. Ruth Alison, Department of Medicine, Nigel Hawkins, Department of Radiation Oncology and Jack Cunningham, Physics Division, retired after many years of service.

In the fall of 1989 we mourned the death of Mrs. Ruth Hartman Frankel, a gracious but determined lady who played a crucial role in developing a volunteer network and programs to support cancer patients and their families. During her lifetime, her courage made a profound difference to the care of patients with cancer. She inspires us to carry on her legacy.

Donald R. Carlow, M.D., C.C.F.P.
President and Chief Executive Officer

TABLE I*

Number of Treatments Given in the PMH Department of Radiotherapy April 1987 - March 1989

EXTERNAL BEAM	1988-1989	1987-1988
Superficial x-ray	792	1,013
Deep x-ray	1,963	2,009
Cobalt	38,716	39,958
Linear accelerators:		
Low energy	8,897	8,433
High energy	27,087	26,986
TOTAL	77,455	78,399
Inpatient treatments	12,235	12,933
Outpatient treatments	65,220	65,466
TOTAL	77,455	78,399
SEALED SOURCES		
Intracavitary	186	235
Interstitial (needles, wires and seeds)	32	32
Strontium applicators	38	65
TOTAL	256	332

*Reprinted with permission, from the Ontario Cancer Institute's Annual Report for 1988-1989.

TABLE II*

Services Provided by PMH at Peripheral Clinics
April 1988 - March 1989

CLINIC	NEW PATIENTS SEEN	TOTAL VISITS
North Bay	128	1,351
Peterborough	6	1,292
Sault Ste. Marie	32	6520
Sudbury	35	941
Timmins	18	959
TOTAL	219	5,163

*Reprinted, with permission, from the Ontario Cancer Institute's Annual Report for 1988-1989.

TABLE III*

Cases of Malignant Disease
Distribution by Site of Malignancy and by Sex
April 1988 to March 1989

SITE	MALE	FEMALE	TOTAL
Head and neck	148	59	207
Ear, nose, throat	236	91	327
Gastrointestinal	447	307	754
Respiratory	622	295	917
Skin	362	230	592
Breast	6	1,341	1,347
Gynecological	–	490	490
Genitourinary	604	62	666
Lymphatic, hematopoietic	365	293	658
Other	312	293	605
TOTAL	3,102	3,461	6,563

*Data generated, with permission, from the Ontario Cancer Institute's Annual Report for 1988-1989.

TABLE IV*

New Patients with Malignant Disease Distribution by Age and Sex
April 1988 to March 1989

SEX	0-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+	TOTAL
Male	33	121	177	248	569	939	616	168	19	2,890
Female	23	129	274	496	705	866	518	168	28	3,207
TOTAL	56	250	451	744	1,274	1,805	1,134	336	47	6,097

*Data generated, with permission, from the Ontario Cancer Institute's Annual Report for 1988-1989.

SPECIAL SERVICES

PROVISION OF SPECIAL DRUGS TO TREAT MALIGNANT DISEASE

The Foundation provides special chemotherapeutic agents to cancer patients who are residents of Ontario and are at home under the care of their doctors. This program was undertaken to assist those patients who find the cost of prolonged therapy with expensive drugs beyond their financial resources.

Drugs can be supplied only if attending doctors complete special prescription forms which are available from the Head Office, any of the Regional Cancer Centres, or the Princess Margaret Hospital. The completed form is mailed to the nearest Foundation centre or the Princess Margaret Hospital and the medication is mailed to the patient. The list of medications provided through the Foundation is available on request.

The total cost of the drug service during the fiscal year April 1, 1988 to March 31, 1989 was $1,010,543.15. During this period 10,497 prescriptions were filled at a cost of approximately $100 per prescription.

TABLE I

Cost of Drug Service
1977-1988/89

Year	Payments for Drugs	Total Cost
1979	257,136.92	261512.36
1980	259,973.32	265,059.36
1981	307,376.30	307,676.97
1982	370,388.28	375,971.20
1983	448,401.93	450,872.94
1984	569,966.52	572,300.25
1985	658,111.38	662,563.20
1986	756,111.56	760,011.54
1987	791,115.85	801,283.70
1988/89*	1,005,064.94	1,010,543.15

*Fiscal year.

CARCINOEMBRYONIC ANTIGEN (CEA) AND STEROID-RECEPTOR ASSAYS PROGRAM

The Ontario Cancer Treatment and Research Foundation is administering and monitoring a program for carcinoembryonic antigen (CEA) and steroid-receptor assays which is funded by the Ministry of Health. The CEA assays for confirmed cases of cancer and the steroid-receptor assays for confirmed cases of breast carcinoma are available, at no charge, to a patient when these assays are performed in the designated laboratories listed below.

Current scientific literature indicates that CEA determinations are useful primarily in patients with cancers arising from the large bowel, breast, or lung. The analytical materials available at present have little utility for tumors of other organs. The only exceptions are cancer of the cervix and medullary cancers of the thyroid.

During the fiscal period April 1, 1988 to March 31, 1989, 5,438 steroid-receptor assays and 53,601 CEA assays have been performed in the designated laboratories.

All laboratories in Ontario are familiar with the program and can provide the details of the data required, sample requirements and specimen transportation. Specimens can be referred to the participating laboratories listed below either directly or through the laboratory which usually provides such services.

Laboratories in the CEA-Assay Program

McMaster University Medical Centre
Dr. E.D. Ryan
1200 Main Street West
Hamilton, Ontario L8S 4J9
tel: (416) 521-2100 ext. 6293

Kingston General Hospital
Dr. M. Raymond
Stuart Street
Kingston, Ontario K7L 2V7
tel: (613) 548-3232 ext. 4185

Victoria Hospital
Dr. E.R. Tustanoff
375 South Street
London, Ontario N6A 4G5
tel: (519) 432-5241

Ottawa Civic Hospital
Dr. C. Lapkoff
1053 Carling Avenue
Ottawa, Ontario K1Y 4E9
tel: (613) 725-4431

General Hospital of Port Arthur
Dr. N. Escott
460 North Court Street
Thunder Bay, Ontario P7A 4X6
tel: (807) 343-6707

Sunnybrook Medical Centre
Dr. A. Malkin
2075 Bayview Avenue
Toronto, Ontario M4N 3M5
tel: (416) 480-4648

Laboratories in the Steroid-Receptor-Assay Program

McMaster University Medical Centre
Dr. E.D. Ryan
1200 Main Street West
Hamilton, Ontario L8S 4J9
tel: (416) 521-2100 ext. 6293

Victoria Hospital
Dr. E.R. Tustanoff
375 South Street
London, Ontario N6A 4G5
tel: (519) 432-5241

Ottawa Civic Hospital
Dr. T. Ooi
1053 Carling Avenue
Ottawa, Ontario K1Y 4E9
tel: (613) 725-4420

Sunnybrook Medical Centre
Dr. D.J.A. Sutherland
2075 Bayview Avenue
Toronto, Ontario M4N 3M5
tel: (416) 487-2722

University of Toronto
Dr. G.E. Mobbs
Medical Sciences Bldg., Rm. 7336
Toronto, Ontario M5S 1A8
tel: (416) 978-3553

DIAGNOSTIC BIOPSY SERVICE AND VOLUNTARY REPORTING BY PATHOLOGISTS

The number of pathology reports voluntarily submitted to the Foundation by the directors of pathology departments increased to approximately 70,000 reports in 1987. These reports are used in the generation of cancer incidence data for Ontario and are most valuable in confirming the diagnosis of new cases. Under The Cancer Act of Ontario, protection is provided for physicians, dentists and hospitals reporting information on cancer cases to the Foundation. The information from the reports is only used for compiling statistics and for carrying out medical and epidemiological research.

The Foundation gratefully acknowledges the continuing co-operation of the participating pathologists and hospitals, and the support of the Ontario Association of Pathologists in the acquisition of these data.

The diagnostic biopsy service pays for biopsies on uninsured patients. In 1988, 6,478 specimens were submitted by dentists (6,178 in 1987).

LODGES FOR AMBULATORY CANCER PATIENTS

At present, the Foundation funds and administers seven lodges for out-of-town ambulatory cancer patients attending the regional cancer centres for diagnosis and treatment. These lodges provide comfortable, supportive accommodation, with minimal supervision, at no cost to the patient. When beds are available, escorts are accommodated at minimal cost.

The Foundation provides this accommodation because the patient often has to travel a considerable distance to reach treatment centres. Without these facilities, the patient would be admitted to hospital at far greater expense to the Province.

Shown below is a list of current facilities and number of beds:

		Number of Beds
HAMILTON	Lakeview Lodge	20
KINGSTON	Quinte-Thousand Islands Lodge	32
LONDON	Thameswood Lodge	48
OTTAWA	Maurice J. Grimes Lodge	60
	Pavillon Alta Vista Lodge	30
THUNDER BAY	Amethyst House Lodge	18
TORONTO	Princess Margaret Hospital Lodge	85

Patients who require hostel accommodation while being treated at the Toronto-Bayview Regional Cancer Centre are housed in the Princess Margaret Hospital Lodge.

TRANSPORTATION OF CANCER PATIENTS

The Foundation covers the cost of transportation to any one of its regional cancer centres or to the Princess Margaret Hospital of those patients who live more than 25 miles from the centre and are considered to be in financial need. For patients 18 years or less, transportation is provided to the principal pediatric oncology treatment centres in the five health science complexes, namely:

HAMILTON	McMaster Medical Centre
KINGSTON	Kingston General and Hotel Dieu Hospitals
LONDON	War Memorial Children's Hospital, Victoria Hospital Corporation
OTTAWA	Children's Hospital of Eastern Ontario
TORONTO	Hospital for Sick Children

Usually transportation is arranged by the local unit of the Canadian Cancer Society, which subsequently is reimbursed by the Foundation.

For the fiscal year ended March 31, 1989, the total cost for transportation of patients was $826,549, compared to 712,647 for the fiscal year ended March 31, 1988.

CANCER INFORMATION SERVICE

In 1988, the Cancer Information Service, funded jointly by the Ontario Cancer Treatment and Research Foundation and the Canadian Cancer Society Ontario Division, continued in its third year of service to the Province of Ontario.

The Service uses the most up-to-date, cancer-related data to provide factual information to our clients. Our database includes information on prevention, early detection, treatment and rehabilitation and educational resources for cancer patients and families. The depth of information varies from patient education material through the latest scientific research articles and the use of the Physician Data Query (PDQ) computerized database from the National Cancer Institute.

Our utilization has increased from 3132 calls in 1987 to 7072 calls in 1989.

The demographic base remains unchanged. The largest group of callers are patients, family members and friends: 15-20% of inquiries are from patients, and 30-40% from family members and friends. Females continue to outnumber male callers 4 to 1.

User surveys indicate that respondents are well satisfied with the service.

Calls are answered Monday to Friday, between the hours 9:00 and 17:00.

The number to call is 1-800-263-6750.

ONTARIO BREAST SCREENING PROGRAM

Recently, Dr. E.A. Clarke presented a proposal for a province-wide, breast screening program on behalf of the Ontario Cancer Treatment and Research Foundation (OCTRF). In May 1989, the Minister of Health, Elinor Caplan, accepted the proposal and announced funding for it. On Sept 1, 1989, Dr. Carl J. Zylak was appointed director of the program.

Clearly, the government intends to deliver a comprehensive, organized and an evaluated breast screening program that will reduce by 40% the incidence of breast cancer – the leading cause of premature deaths in women between 50 and 64 years of age. In accordance with Ontario's health goals, the OCTRF has committed itself to a program which is sensitive to women's needs, builds on health-promoting behaviours and fosters full partnership between all interest groups in the community.

The screening maneuver consists of two parts: two-view mammography of each breast and physical examination by nurse examiners every two years. Women in the target group, ages 50 to 64, can enter the program through three routes: by letters of invitation from the program, by direct referral from the patient's physician, and by self-referral, if the patient identifies herself with a family physician. Women will remain in the program until their 70th birthday. A major objective of the program is a compliance rate of 70%.

The OCTRF will deliver this program through its existing regional cancer centres. Currently, there are eight such centres in Ontario and the Princess Margaret Hospital has agreed to function as the ninth "centre". Each region will be responsible for establishing sites, of a number and location, fixed and/or mobile, necessary to ensure access to screening every two years by women in the target age group.

A dedicated screening centre will accommodate at least 10,000 women per year. The appropriate ambiance will be staffed by dedicated, caring individuals. Available here will be educational materials in written and audiovisual form pertaining to breast self-examination. The teaching and evaluation of breast self-examination is not part of the program. The principal challenges facing the organizers concern recruitment of the women in the target age group and the delivery of a quality service by dedicated, skillful professionals. The sponsors will recruit individuals with expertise in health promotion and in the community-based approach to coalition building, both centrally and regionally.

Also, the Ministry and the new Ontario Cancer Control Agency need to develop educational programs to orient physicians to the delivery of health care via this public health model, as opposed to the case-finding model. Such programs will form the basis for an on-going dialogue.

We anticipate that in the prevalent round of screening, we will identify enough mammographic abnormalities to produce a recall rate of 7-10%. A recall rate in the 6-8% range will result for the abnormalities detected on physical examination by the nurse examiner. In every case, the patient and the patient's physician will be notified of the findings. Each region is free to determine the best program for the management of women with screen-detected abnormalities. Undoubtedly, some physicians will wish to assume complete responsibility for management, that is, take control of the patient during assessment and subsequent operation that is needed. Those regions and communities that already have breast assessment centres and/or clinics will provide prompt referral for these anxious women. Some regions may wish to complete the assessment in the screening centre itself, then the patient is assessed by a clinician and a radiologist jointly, sharing appropriate work-up and decision-making. If a woman needs a biopsy, her family would be consulted with respect to definitive referral. Whatever approach is taken, the program is responsible for making the provisional diagnosis, for recording the findings, for sending out requests for follow-up information, once we have determined an appropriate interval. One of the major challenges of this program is to guarantee access to appropriate assessment for women with screen-detected abnormalities.

The Ontario Breast Screening Program is an ambitious undertaking. Its goal is to have a dedicated screening centre in each of the nine regions within the calendar year or by the end of the first quarter of 1991. Success of the program depends in large measure on recruitment of the women in the target age group and the delivery of quality service by dedicated professionals. This dedication is a necessary prerequisite if this program is to achieve its goal – a 40% reduction in mortality from breast cancer in the Province of Ontario.

RESEARCH PROGRAMS

SUMMARY OF OCTRF RESEARCH

There are three programs funded through the research budget of the Foundation: one, Career Investigators; two, Research Unit, Division of Epidemiology and Statistics; and three, the Ontario Clinical Oncology Group. In addition there is laboratory and clinical research carried out by medical and radiation oncologists and by physicists all of whose salaries come from the service budget of the Foundation. Finally, much of the operating support for all of the Foundation's research is peer reviewed and comes from external granting agencies, e.g., National Cancer Institute of Canada, Medical Research Council of Canada, and Ontario Ministry of Health; this support totalled over 5 million dollars in 1989.

The following is a brief description of the three programs funded through the Foundation's research budget.

Career Investigators (Career Scientists, Research Associates, Research Scholars and Clinician Scientists)

During 1989, the Foundation provided salary and core support for 11 career scientists: Dr. G. Singh in Hamilton; Drs. S.P.C Cole, J. Gerlach and J.C. Kennedy in Kingston; Drs. A. Chambers, J. Harris, W.R. Inch and J. Koropatnick in London; and Drs. H.C. Birnboim, R.G. Hawley and R.G. Liteplo in Ottawa; 5 research associates at the University of Toronto: Drs. M.A. Baker, J.G. Connolly, B.L. Gallie, H.F. Haberman and G.E. Mobbs; and 2 research scholars: Dr. G.L. Hammond in London and Dr. J.C. Kudlow at the University of Toronto. The Foundation also provided core grants to cover such items as secretarial support for five clinician scientists: Drs. H. Hirte (Hamilton), B. Campling (Kingston), D. Logan (Ottawa), N. Berinstein and N. Lassam (Toronto-Bayview).

Research Unit, Division of Epidemiology and Statistics

The Foundation provides infrastructure support for the Research Unit of the Division of Epidemiology and Statistics. Members of the Division, which has been affiliated with the Department of Preventive Medicine and Biostatistics at the University of Toronto since 1978, compete for research operating funds through the various external granting agencies. In addition to their individual research pursuits, they assist research workers throughout the Province by providing epidemiological and biostatistical information, by responding to requests from the Ministry of Health on relevant issues, and by providing information to the scientific community and general public.

The Ontario Clinical Oncology Group (OCOG)

Submitted by Dr. P.B. McCulloch

OCOG, a province-wide clinical trials group, has initiated and coordinated a number of studies involving the OCTRF Regional Cancer Centres, the Ontario Cancer Institute and university medical schools.

Our first trial comparing conservative therapy alone ("lumpectomy") with adjuvant radiotherapy following the lumpectomy in surgically staged, pathologically node-negative breast cancer patients was initiated in 1984, the year after OCOG was founded. In early 1989 when it closed, it had a sample size of over 835 patients. The Princess Margaret Hospital in Toronto and the OCTRF Regional Cancer Centres in Hamilton, London, Ottawa, Thunder Bay and Windsor accrued these patients. The first report from this trial will be presented at the American Society of Clinical Oncology meeting in May 1990.

Higher-risk (Stage II) breast-cancer patients have been studied in two consecutive trials. We have reported the first trial of adjuvant therapy, which was initiated in 1984 and closed in 1987 (430 patients). In the second trial, initiated in 1988 and closed in 1989, over 100 patients from five OCTRF Regional Cancer Centres participated in a study to determine the effective dose for the combination 5-FU, epirubicin and cyclophosphamide. The large, randomized, National Cancer Institute of Canada Clinical Trials Group study across Canada is now studying this dose schedule. Thus Ontario investigators did the pilot study and gained valuable experience in an experimental adjuvant chemotherapy, which now is being compared to standard adjuvant chemotherapy in a national trial.

We are studying the chemoprophylaxis of lung cancer. Over 120 volunteers have been accrued into a randomized double-blind study of etretinate, a Vitamin A derivative, which attempts to reverse the metaplasia detected in the sputum of long-term cigarette smokers.

In 1988, a study was initiated in eight Ontario centres to determine the value of medroxyprogesterone and wide-field radiotherapy in high-risk, localized endometrial cancer. However this study was suspended because of slow accrual and the province's crisis in radiotherapy.

A high incidence of venous thrombosis was detected in patients entered into the initial trial of adjuvant chemotherapy of Stage II breast cancer. Now investigators in seven Ontario centres are entering patients into a double-blind randomized trial of warfarin to decrease the incidence of such thrombosis in patients with metastatic breast cancer beginning palliative chemotherapy.

In 1988, neurosurgeons at four Ontario cancer centres and several affiliated hospitals began to enter patients into a study to define the role of surgery in the treatment of solitary brain metastases.

In February 1990, OCOG will hold the fifth annual three-day workshop on clinical investigation in the Department of Clinical Epidemiology and Biostatistics at McMaster University. As in the past years, there will be 20 participants from the OCTRF Regional Cancer Centres, the Ontario Cancer Institute and Ontario medical schools. Each year, three tutorial groups put forward a number of research ideas for detailed discussion. Each of the four previous workshops developed at least one research question, which attracted peer-reviewed funding from a national granting agency. Most of the participants believe that this enjoyable education experience has furthered their scientific careers.

In the spring of 1989, OCOG was granted a further three years of funding from the Ontario Ministry of Health and the OCTRF. In late 1989 and early 1990, Drs. Levine and McCulloch from the group's Head Office visited most of the provincial regional cancer centres to discuss future directions.

Senior Scientific Staff at the Ontario Cancer Institute

In addition to the funding of the three programs just described, the Foundation is the conduit through which the provincial government provides salary and core support for the senior scientific staff at the Ontario Cancer Institute. The annual research report of the Ontario Cancer Institute describes the projects carried out by these scientists.

J.C. Laidlaw, M.D.

RESEARCH PERSONNEL SUPPORTED BY OCTRF

Career Scientists

Hamilton Regional Cancer Centre:

G. Singh, Ph.D

Kingston Regional Cancer Centre:

S.P.C. Cole, Ph.D
J.H. Gerlach, Ph.D
J.C. Kennedy, M.D

London Regional Cancer Centre:

A.D. Chambers, Ph.D
J. Harris, Ph.D
W.R. Inch, Ph.D
D.J. Koropatnick, Ph.D

Ottawa Regional Cancer Centre:

H.C. Birnboim, M.D
R.G. Hawley, Ph.D
R.G. Liteplo, Ph.D

Clinician Scientists

Hamilton Regional Cancer Centre:

H. Hirte, M.D

Kingston Regional Cancer Centre:

B. Campling, Ph.D

Ottawa Regional Cancer Centre:

D. Logan, M.D

Toronto-Bayview Regional Cancer Centre:

N. Berinstein, M.D
H. Lassam, M.D

Research Associates

Toronto General Hospital:

M.A. Baker, M.D
(to June/89)

Toronto Western Hospital:

H.F. Haberman, M.D

University of Toronto:

J.G. Connolly, M.D
(to Nov/89)
B.L. Gallie, M.D
G.E. Mobbs, Ph.D

Research Scholars

University of Western Ontario:

G.L. Hammond, M.D

University of Toronto:

J.E. Kudlow, M.D
(to Aug/89)

REPORTS ON RESEARCH PROJECTS

HAMILTON

Hamilton Regional Cancer Centre:

Distinct Genomic Copy Number in Mitochondria of Different Mammalian Organs
G. Singh **111**

Studies on the Mechanisms of Cancer Metastasis to Bone
G. Singh and F.W. Orr **112**

Additional Investigations **113**

KINGSTON

Kingston Regional Cancer Centre:

Photodynamic Therapy for Cancer
J.C. Kennedy **117**

Multidrug Resistance: Topography and Molecular Interactions of P-Glycoprotein
J.H. Gerlach **118**

Multidrug Resistance in Human Lung Cancer
S.P.C. Cole **119**

Clinical Application of the MTT Assay
B.G. Campling and Y-M. Lam **120**

Clinical Drug Resistance in Small-Cell Lung Cancer
B.G. Campling **121**

LONDON

London Regional Cancer Centre:

Use of Magnetic Resonance Spectroscopy (MRS) to Monitor Radiotoxicity Caused by Adriamycin and Protection by ADR-529
W.R. Inch, S.E. Daly, E.R. Tustanoff and T.T. Thompson **122**

Metallothionein Expression and Resistance to Radiation and Chemotherapeutic Drug Treatment
J. Koropatnick, M.G. Cherian and E. Cairney 124

Preparation of Monoclonal Antibodies Against Metallothionein
J. Koropatnick and J.F. Harris 125

Somatic Cell Genetic Analysis of Metastatic Cells
J.F. Harris and A.F. Chambers 126

Contribution of Oncogenes to Tumor Metastasis
A.F. Chambers 128

Stability of Human Monoclonal Antibody Production in Mouse-Human Hybridoma Cells
J. Koropatnick and J.F. Harris 130

Development and Characterization of Monoclonal Antibodies to Metastatic Tumor Cells
J.F. Harris 132

Structure/Function and Hormonal Regulation of Plasma Steroid Binding Proteins
G.L. Hammond 134

Additional Investigations 136

OTTAWA

Ottawa Regional Cancer Centre:

Mechanism of Oxygen-Radical Damage to Cellular DNA and Its Role in Tumor Promotion and Tumor Progression
H.C. Birnboim 138

Sites of DNA Strand Breaks in PMA-Stimulated Human Granulocytes
H.C. Birnboim 140

In Vitro and In Vivo Induction by Granulocyte-Derived Oxyradicals of Mutants at the HPRT Locus in Mouse Cells
H.C. Birnboim 141

Alterations in Methionine Metabolism Associated with Tumor Progression
R.G. Liteplo 143

Signal Transduction Processes Associated with the Mitogenic Response
R.G. Liteplo 144

Role of Interleukin-6 in B-Cell Neoplasia
R.G. Hawley 145

Regulation of Hematopoiesis by Interleukin-1α
R.G. Hawley 146

Expression of Platelet-Derived Growth Factor Gene in the Baculovirus
D.M. Logan and C-Y. Kang 147

Kaposi's Sarcoma — An In Vitro Study
D.M. Logan, C.A. Izaguirre, L.B. Huebsch and C-Y. Kang 148

Additional Investigations 149

THUNDER BAY

Thunder Bay Regional Cancer Centre:

Clinical Investigations 154

TORONTO

Toronto-Bayview Regional Cancer Centre:

Analysis and Management of B Cell Lymphomas
N.L. Berinstein 157

Additional Investigations 159

Division of Epidemiology and Statistics:

Epidemiology Research Unit
E.A. Clarke, E. Holowaty, N. Kreiger, L.D. Marrett and J. McLaughlin 166

Additional Investigations 168

University of Toronto:

Factors Affecting Urinary Mutagenic Levels of Workers with Bladder Cancer
B.C.K. Choi and J.G. Connolly 176

Relationship of Pheomelanin and Photosensitizers to Skin Cancer
H.F. Haberman and I.A. Menon 177

Hormone Receptor Mechanisms in the Development and Treatment of Prostatic Neoplasia
G.E. Mobbs 178

WINDSOR

Windsor Regional Cancer Centre:

Clinical Investigations 180

Hamilton Regional Cancer Centre

DISTINCT GENOMIC COPY NUMBER IN MITOCHONDRIA OF DIFFERENT MAMMALIAN ORGANS*

G. SINGH**, *Hamilton, Ontario*

The present investigation was undertaken to quantitate mtDNA in mitochondria from various mouse organs. Mitochondrial density was determined by stereological analysis of tissue sections using electron microscopy. mtDNA was analyzed from each organ using a specific mtDNA probe. This is an important advance because, in the early 1960s, these probes were not available and hence results from earlier studies may reflect contamination with nuclear DNA. Nonspecific contamination may account for many discrepancies.

This study has established that mitochondria in liver, kidney, heart and brain of the mouse have a distinct mitochondrial density. Also it has shown that the mtDNA copy number per mitochondrion is organ-specific. This is the first comprehensive examination of mitochondrial density and quantitation of mitochondrial genomes in mouse organs. It demonstrates variability not only in mitochondrial density but also in genomic copy number in mitochondria of various tissues. This information is useful in delineating organ-specific toxicities by various chemotherapeutic agents at the mechanistic level.

This project is supported by a grant from the Medical Research Council of Canada.

---

*CS-106-4.

**Career Scientist, OCTRF Hamilton Regional Cancer Centre; and Assistant Professor of Pathology, McMaster University, Hamilton.

STUDIES ON THE MECHANISMS OF CANCER METASTASIS TO BONE*

G. SINGH** and F.W. ORR†, *Hamilton, Ontario*

Earlier we reported that the resorption of bone in an organ culture system releases factors, which stimulate the chemotactic migration and growth of cells from the Walker 256 (W256) carcinosarcoma, an experimental rat tumor with a propensity to metastasize to bone. We have shown that TGF-beta accounts for a significant proportion of the migratory and growth-promoting activity in conditioned media. Thus we postulate that bone metastasis is regulated by local bone-derived factors (including TGF-beta) whose production is coupled with bone-remodelling activity.

Since many workers have linked activation of oncogenes *(myc, sis, ras, erbB)* to metastasis and to the cellular response to many growth factors, we will examine the levels of these oncogene mRNAs and look for expression of their products in W256 cells at various times after incubation with TGF-beta or bone culture medium. Preliminary data indicate that *c-myc* mRNA is increased from control levels within 1 hr of placing W256 cells in media with either growth factor. On the basis of these experiments, we hope to identify oncogenes which are relevant to the local response of cancers to the environment in bone.

Finally, we will look for correlations between TGF-beta production and tumor growth rate in vivo, using a model of lung injury in which others have shown increased TGF-beta and in which we demonstrated increased rates of tumor growth in metastases compared to the primary.

---

[*] CS-106-5.

[**] Career Scientist, OCTRF Hamilton Regional Cancer Centre; and Assistant Professor of Pathology, McMaster University, Hamilton.

[†] Professor of Pathology, McMaster University.

ADDITIONAL INVESTIGATIONS

Dr. W.M. Hryniuk, Chief Executive Officer HRCC and Vice-President OCTRF, reports on the following clinical research investigations:

Under the guidance of Dr. Brian Wilson, Director of Research, and Dr. Mark Levine, Head of Clinical Trials, our research program continues to develop new methods of treatment and to raise existing standards. This interaction of investigators from Henderson Hospital and McMaster University emphasizes our commitment to the development of a comprehensive cancer centre research environment. Examples are:

- Studies of new modes of treatment: photodynamic therapy, radioimmunotherapy, hyperthermia, and biologic response modifiers (BRM).
- Preventive and clinical therapeutic trials.
- Development of laboratory assays of therapeutic response.
- Studies of the mechanisms of metastasis.

Over the past decade, with the OCTRF support, our Centre has made considerable progress in building up a cadre of independent basic researchers and clinician scientists. In 1988, the Hamilton Civic Hospitals opened a dedicated research centre at the Henderson Hospital, under the directorship of Dr. Jack Hirsh. This initiative will further these collaborative efforts and contribute to improved treatment.

Joint Cancer Centre/Hospital Research Institute projects are underway in several areas related to thromboembolism and clinical trials methodology. For example, Dr. Mark Levine is collaborating with members of the Institute in delineating the role of prophylactic anticoagulants in adjuvant chemotherapy of Stage II breast cancer; Dr. Brian Wilson is investigating the medical applications of lasers; and Drs. D.I. Hodson and G. Singh in exploring those areas of overlap between cancer metastasis and the vascular system.

These strong links between basic and clinical studies have fostered new clinical trials in several disease sites. In particular, laboratory data are being applied directly to the design of clinical treatments. Thus, in head and neck cancer, clinical trials of therapeutic response are strengthened by in vitro assays of tumor-cell proliferation, by correlations between the levels of antineoplastic drugs and radiation toxicity, and by "quality of life" indices. Other examples of such links are found in studies of the use of BRM-labelled monoclonal antibodies in the detection of ovarian cancer; on the application of photodynamic therapy for lung, brain, gastrointestinal tract and skin cancer; and on radioimmunotherapy for malignant melanoma. Some of these basic and clinical studies are multicentre (they include other OCTRF Regional Cancer Centres), are multidisciplinary and are funded entirely by peer-reviewed research grants. Current terms range from one to four years. As of May 1988, the following peer-reviewed grants are held by the Hamilton Centre staff members.

NAME	TITLE OF PROJECT	AGENCY
ARNOLD, LEVINE BROWMAN, HRYNIUK NEWHOUSE, D'SOUZA	Synthetic Retinoid or Retinate Effects on Squamous Metaplasia	OMH
BROWMAN	Determinants of Response in Acute Leukemia	NCI
BROWMAN	Morphologic Assessment of Drug Resistance in Human Tumor Fragments	PSI
BROWMAN, LEVINE HODSON, CRIPPS	Trial of Concurrent Infusional 5-FU Chemotherapy with Standard Radical Radiation Therapy in Locally Advanced Head and Neck Cancer	NCIC
CLARK, HIRTE	Factors Determining Susceptibility of Clonogenic Human Ovarian Carcinoma Cells to Lysis by Cytokine-Activated Host Effector Cells	NCIC
HIRSH, LEVINE, GENT	re-PA in Pulmonary Embolism	OMH
KWOK	Electron Dosimetry in Heterogenous Media	NSERC
KWOK	Electron Dosimetry in Radioimmunotherapy	NIH
KWOK, NEVILLE	Radioimmunotherapy of Human Malignant Melanoma using Multicell Spheroids and Xenographs as Models	NCIC
LEVINE, BUSH HRYNIUK, GENT	Adjuvant Chemotherapy for Stage II Breast Cancer	MRCC
LEVINE, HIRSCH GENT, TURPIE	Clinical Trial of Low Molecular Weight Heparin	HSFO

NAME	TITLE OF PROJECT	AGENCY
LEVINE, HIRSCH GENT, WEITZ	The Optimal Duration of Oral Anticoajulant Therapy in Patients with Deep-Vein Thrombosis	OMH
LEVINE, HIRSCH WEITZ, ANDREW	Trial Monitoring of Heparin Therapy in Patients with Heparin Resistance	HSFO
MULLER, WILSON	A Phase I/II Trial of Photodynamic Therapy of Malignant Brain Tumors	NCIC
NEVILLE, SAUDER KWOK	Whole-Body Hyperthermia in Combination with Nitrosourea or Immunotherapy in Human Malignant Melanoma Nude Mouse Xenograft	NCIC
ORR	Free-radical-Mediated Mechanisms in Cancer Metastasis	NCIC
ORR, BUCHANAN	Regulation of the Interactions Between Endothelium and Tumor Cells	MRCC
ORR, SINGH	Studies on the Mechanisms of Cancer Metastasis to Bone	MRCC
RATHBONE	Unique Cell-Growth Factors from Human Brain Tumors	NCIC
SINGH	Mitochondrial DNA as a Critical Target for Toxicity Caused by Antineoplastic Drugs	MRCC
TURPIE, GENT HIRSCH, LEVINE	Trial of Recombinant Human-Tissue-Type Plasminogen Activator in Patients with Deep-Vein Thrombosis	MRCC

NAME	TITLE OF PROJECT	AGENCY
WILSON, FIRNAU ORR	Radiolabelling of Hematoporphyrin Derivative for in vivo Quantitation during Photodynamic Therapy	NCIC
WILSON, PATTERSON	Development and Application of Light Dosimetry for Photodynamic Therapy	NCIC
WILSON, PATTERSON WYMAN	Medical Laser Applications	OLLRC

A major resource in carrying out these multidisciplinary basic/clinical studies is the Hamilton Regional Cancer Centre Clinical Trials Unit. This group supervises the execution of ongoing clinical trials, gives advice about methods to investigators at the Centre, both in design and analysis of trainees in medical, radiation and surgical oncology and hematology. This group, under the direction of Dr. Mark Levine, provides leadership in the conduct of sound clinical research in patients with malignant disease. To a large extent, the department depends on external funding from granting agencies, the National Cancer Institute of Canada, and the pharmaceutical industry. Over 500 patients are being followed on various local, regional and national trials and Phase II studies in the following disease sites: bladder, breast, endometrium, head and neck, Hodgkin's disease, lung, leukemia, lymphoma, mesothelioma, myeloma, ovary and sarcoma. In addition, symptom control studies are beginning to show a reduction in nausea and vomiting in ovarian patients receiving high-dose cisplatin. These results encourage us to study anti-emetic measures in patients with cancer in other sites, which require high-dose chemotherapy.

Kingston Regional Cancer Centre

PHOTODYNAMIC THERAPY FOR CANCER*

J.C. KENNEDY**, *Kingston, Ontario*

The ultimate objective of our group is to improve photodynamic therapy for cancer. Our research has been directed toward the discovery of better tissue photosensitizers – ones that have low toxicity, low neurotoxicity, high specificity for malignant tissues, rapid clearance from the skin and other normal tissues, and an excitation spectrum that includes the far red and/or very near infrared. Our immediate goal has been to identify the mechanisms responsible for the tumor specificity shown by three quite different kinds of cell/tissue photosensitizers and then to use that knowledge to select or synthesize improved photochemotherapeutic agents. The process has involved ongoing collaboration with faculty at the University of Quebec at Trois Rivieres (organic synthesis), the University of Sherbrooke (photochemistry), and the University of Padova, Italy (pharmacokinetics). Progress to date has been good. We have obtained good evidence that the tumor specificity shown by several different types of carboxylic acid porphyrins can be greatly influenced by both the pH of the extracellular fluid and the solubility of the porphyrin in water. In addition, we have evidence that the tissue specificity shown by sulfonated photosensitizers depends upon a quite different mechanism, one that requires enzymatic activity as well as specific environmental conditions. At the applied level, we have developed and are evaluating clinically a new photochemotherapeutic agent, ALA-induced protoporphyrin IX (Queen's University/Royal Military College patent pending). Another photosensitizer (to be patented), which was synthesized in collaboration with the University of Quebec in Trois Rivieres, combines low toxicity with a strong chemotherapeutic (dark) effect upon certain types of tumors in mice.

These projects are supported by grants from the National Cancer Institute of Canada, the Department of National Defence, and the Physicians' Services Incorporated Foundation.

---

* CS-101.

** Career Scientist, OCTRF Kingston Regional Cancer Centre; Associate Professor of Oncology and Pathology, Queen's University; and Adjunct Associate Professor of Chemistry and Chemical Engineering, Royal Military College, Kingston.

MULTIDRUG RESISTANCE: TOPOGRAPHY AND MOLECULAR INTERACTIONS OF P-GLYCOPROTEIN*

J.H. GERLACH**, *Kingston, Ontario*

Simultaneous resistance to multiple agents continues to be a major limiting factor in the control of tumors with combination chemotherapy. With a better understanding of the molecular basis of multidrug resistance (MDR), we might devise new regimes based on the circumvention of MDR or on the elimination of cells expressing the MDR phenotype. These present studies will help provide such an understanding of the best characterized form of MDR – that mediated by P-glycoprotein. This moiety is a high-molecular weight, plasma-membrane glycoprotein that is overexpressed in multidrug-resistant cells and functions as an ATP-dependent, drug-export pump. Resistance is thought to result from lower intracellular drug concentrations in cells overexpressing P-glycoprotein. The specific goals of the proposed research are:

1. *Generation of multidrug resistance mutants with altered P-glycoprotein function resulting from interaction with other membrane components.* The mutants will be selected in a manner which maintains the expression of P-glycoprotein but which results in the loss of major facets of the multidrug resistance phenotype. Such "partial revertants" may result from mutations within the P-glycoprotein gene or as the result of the generation of "suppressor" mutants in components interacting with and modulating the activity of P-glycoprotein.
2. *Characterization of membrane topography of P-glycoprotein in the plasma membrane with regard to tertiary structure of transmembrane domains.* The use of lipophilic, photoreactive probes will permit the labelling of amino acids buried in the plasma membrane. These probes also will be used to cross-link closely associated regions of the protein. Analysis of the products of such reactions will provide information on the structure of membrane proteins like P-glycoprotein.
3. *Identification of interactions of P-glycoprotein with other components of the plasma membrane as detected by photoreactive probes and "cross-linkers".* The "neighbours" of P-glycoprotein will be identified through the use of bifunctional cross-linking agents and by selective solubilization of membrane components. A major unanswered question concerns the stoichiometry of P-glycoprotein in the plasma membrane because the quaternary structure is unknown. It may well be that P-glycoprotein is its own closest neighbour.

These experiments will provide the foundation for a greater understanding of the function of P-glycoprotein both as an independent molecule and as it functions in the environment of the plasma membrane. Such information will increase our understanding of the role P-glycoprotein plays in MDR as well as increasing our knowledge of an intriguing, plasma-membrane-transport molecule.

This research is supported by grants from the Cancer Research Society, Inc., and the Clare Nelson Bequest of the Kingston General Hospital, Inc.

---

* CS-109.

** Career Scientist, OCTRF Kingston Regional Cancer Centre; and Assistant Professor of Oncology, and Biochemistry, Queen's University, Kingston.

MULTIDRUG RESISTANCE IN HUMAN LUNG CANCER*

S.P.C. COLE**, *Kingston, Ontario*

One of the major reasons for treatment failure in initially responsive small-cell lung cancer (SCLC) is the appearance and proliferation of multidrug-resistant tumor cells. A stable resistant SCLC cell line, designated H69AR, has been isolated in my laboratory using Adriamycin as the selecting agent. In addition to Adriamycin, the H69AR cell line is cross-resistant to a panel of structurally diverse drugs and thus possesses the multidrug resistance phenotype. This cell line is unusual in that it does not overexpress P-glycoprotein, a plasma membrane efflux pump commonly associated with the development of multidrug resistance. The major focus of my research is the investigation of non-P-glycoprotein-mediated multidrug resistance using the H69AR cell line as a model system.

The H69AR cell line has been used to generate monoclonal antibodies and we are investigating the specificity of these antibodies using a variety of immunological techniques. We continue with the biochemical characterization of the antigens detected by these antibodies and are elucidating the mechanism(s) of resistance in H69AR cells in a number of ways. Firstly, the pharmacokinetic properties (rates of drug uptake, efflux and accumulation) are being examined using isotope methods. Secondly, using filter elution techniques, we are testing the possibility that drugs cause less DNA damage in H69AR cells as well as having an enhanced ability to repair DNA damage. DNA topoisomerase II activities are being measured to see if they might also be involved in resistance. Thirdly, we are investigating the role of glutathione and associated enzymes because they have been shown to play a crucial protective role against cellular injury. Lastly, we have begun to examine the molecular basis of resistance in H69AR cells using recombinant DNA technology.

While it is important to understand the basis of drug resistance, the circumvention of drug resistance would have an immediate major impact on the treatment of many human cancers. We have collaborated with a number of medicinal chemists and pharmaceutical companies to test the ability of commercially available drugs and investigational new drugs to circumvent resistance or enhance the chemosensitivity of H69AR cells.

This project is funded by the National Cancer Institute of Canada.

---

* CS-107-1.

** Career Scientist, OCTRF Kingston Regional Cancer Centre; and Associate Professor of Oncology, and Pharmacology and Toxicology, Queen's University, Kingston.

CLINICAL APPLICATION OF THE MTT ASSAY*

B.G. CAMPLING** and Y-M. LAM†, *Kingston, Ontario*

We have adapted a simple colorimetric test, the MTT assay, for chemosensitivity testing of human cancer cell lines and fresh human tumors. The major advantages of this assay over other tests of drug sensitivity are its speed and simplicity. We have used the MTT assay to measure the chemosensitivity of a panel of 16 lung cancer cell lines and a variety of clinical samples including solid tumors, effusions and human leukemic blast cells.

Twenty-five different chemotherapeutic agents have been tested for cytotoxicity to human tumor cells and all but five were active in this system. We have developed methods for storage, graphical presentation and statistical analysis of the large amounts of data generated by this assay.

We propose to introduce further improvements in the method, so that it can be used routinely for chemosensitivity testing of human tumors. We hope to develop methods for separating tumor cells from non-tumor cells in samples of solid tumors and effusions and to establish definitions of in vitro sensitivity and resistance. Then we will undertake a prospective clinical trial of chemosensitivity testing in acute leukemia to determine whether the assay predicts clinical response.

Mathematical and statistical techniques, known collectively as response surface methodology, will be used to examine interactions between chemotherapeutic agents. In addition, these methods will be used to examine the effects of a variety of non-chemotherapeutic agents, which are reported to enhance sensitivity to chemotherapy. A multivariate statistical technique, cluster analysis, will be applied to examine patterns of drug sensitivity and resistance in human tumor cell lines and clinical samples. This method will also be used to examine relationships between chemotherapeutic agents.

Thus, we have shown that it is feasible to use this new assay for clinical chemosensitivity testing. While we are working on further improvements in this method, we will undertake a prospective clinical trial of chemosensitivity testing using this assay.

This project is supported by a grant from the Cancer Research Society, Inc.

---

* CLS-002.

** Clinician Scientist, OCTRF Kingston Regional Cancer Centre; and Assistant Professor of Oncology and Medicine, Queen's University, Kingston.

† Assistant Professor, Department of Community Health and Epidemiology, Queen's University.

CLINICAL DRUG RESISTANCE IN SMALL-CELL LUNG CANCER*

B.G. CAMPLING**, *Kingston, Ontario*

Lung cancer is the major cause of cancer-related death in North America; small-cell lung cancer (SCLC) accounts for 20-25% of these deaths. Combination chemotherapy is the primary mode of management in SCLC and the development of resistance to chemotherapy is the major reason for treatment failure. In many situations in vitro and in vivo, resistance to multiple chemotherapeutic agents is related to the overexpression of a unique membrane protein, P-glycoprotein (P-gp). However, there is now substantial evidence that the presence of P-gp is uncommon in patients with multidrug resistant SCLC.

Two hypotheses have been advanced to explain the infrequent expression of P-gp in multidrug resistant SCLC: 1) the assays used to detect this protein have not been sensitive enough to detect low levels of expression, which may be clinically significant; and 2) in this histological type, other mechanisms of multidrug resistance may be relatively more important.

Two approaches will be taken to investigate the first hypothesis: Firstly, an extremely sensitive molecular technique, using the polymerase chain reaction, will be employed to detect P-gp expression in a panel of SCLC cell lines developed in this laboratory. These studies will be done in collaboration with Dr. J. Gerlach. Secondly, a highly sensitive immunohistochemical technique, developed by Dr. H.S.L. Chan, will be used to detect P-gp expression in these SCLC cell lines.

Two approaches will be taken to investigate the second hypothesis: Firstly, we will examine our cell lines for reactivity with monoclonal antibodies, developed in Dr. S.P.C. Cole's laboratory; these detect multidrug resistance-associated antigens unrelated to P-gp. Secondly, we will investigate the role of glutathione and glutathione-related enzymes in our SCLC cell lines.

Once the methods are well established, the results in SCLC cell lines will be compared to the original tissue samples from which the cell lines were established. Then we will undertake retrospective and prospective studies on clinical samples.

The goal of these studies is to develop assays of drug sensitivity and resistance, which may be of clinical utility and will lead to a better understanding of clinically important mechanisms of resistance in SCLC. This work will lead to prospective studies correlating expression of resistance-associated markers with response to chemotherapy and to new approaches to reversing drug resistance.

This project is funded by Physicians' Services Incorporated Foundation, and the Ontario Respiratory Disease Foundation.

---

*CLS-002-1.

**Clinician Scientist, OCTRF Kingston Regional Cancer Centre; and Assistant Professor of Oncology and Medicine, Queen's University, Kingston.

London Regional Cancer Centre

USE OF MAGNETIC RESONANCE SPECTROSCOPY (MRS) TO MONITOR CARDIOTOXICITY CAUSED BY ADRIAMYCIN AND PROTECTION BY ADR-529*

W.R. INCH**, S.E. DALY†, E.R. TUSTANOFF†† and T.T. THOMPSON‡
London, Ontario

The therapeutic use of Adriamycin is limited by its cardiotoxic effect, which may be acute, occuring within minutes of its administration, or chronic, developing several weeks or months later[1]. The latter effect can be extremely debilitating and even cause death[2]. Topical magnetic resonance spectroscopy (MRS) allows us to measure in intact tissues, a number of biochemical parameters, which otherwise are recognized only by destructive tissue analysis. Victoria Hospital has a spectrometer, which is capable of detecting proton (H-1), carbon (C-13) and phosphorus (P-31) resonance. Because the phosphorus atom is associated with molecules involved in energy production, this non-invasive technique can be applied to studies of cardiac metabolism.

We have developed an animal model to study Adriamycin-induced cardiotoxicity using New Zealand white rabbits. We have shown a correlation between the severity of the cardiomyopathy and the ratio of inorganic phosphorus-to-adenosine triphosphate. Thirty-six rabbits will be entered into the study; these will be divided into three groups: Control, Adriamycin, Adriamycin and ADR-529 [(S)-(+)-bis-4,4'-(1 methyl-1,2-ethane-diyl)2,6-piperazinedione][3]. Group II and III will receive Adriamycin at a rate of 24 mg/kg/week intravenously; Group III will also receive 15 mg/kg/week ADR-529. Group I, the control group, will receive an equivalent volume of saline.

We will obtain baseline P-31 spectra of the heart and skeletal muscle before drug administration and at various times up to 10 weeks (total dose Adriamycin 24 mg/kg). The electrocardiogram will be recorded at regular intervals. Histologic sections of the heart will be examined at intervals up to 10 weeks using representative animals from each group.

The data will be analyzed to see if the protection afforded by ADR-529 is reflected in the cardiac high-energy phosphates. If so, P-31 MRS could provide an non-invasive technique to monitor the degree of Adriamycin-induced cardiomyopathy.

---

*CS-100-1.

**Career Scientist, OCTRF London Regional Cancer Centre; and Professor of Oncology and Medical Biophysics, University of Western Ontario, London.

†Graduate Student, Department of Biochemistry, UWO.

††Professor of Biochemistry, UWO.

‡Assistant Professor of Radiology and Nuclear Medicine, UWO.

REFERENCES

1. Dorshow JH, Locker GY, Myers CE: Doxorubicin. Toxicity: The interaction of drug and endogenous defence against free radical attack. *Clin Res* 1978; **26:** 434.
2. Carter SK: A review. *J Natl Cancer Inst* 1979; **63:** 855.
3. Speyer JL, Green MD, Kramer E et al: Protective effect of the bispiperazinedione ICRF-187 against doxorubicin-induced cardiac toxicity in women with advanced breast cancer. *N Engl J Med* 1988; **319:** 745.

METALLOTHIONEIN EXPRESSION AND RESISTANCE TO RADIATION AND CHEMOTHERAPEUTIC DRUG TREATMENT*

J. KOROPATNICK**, M.G. CHERIAN† and E. CAIRNEY††,
London, Ontario

The development of resistance to radiation or chemotherapy by malignant cells is a significant cause of failure of cancer therapy. Metallothioneins (MTs) are a class of proteins that have been associated with resistance to radiation and chemotherapeutic agents. It is hypothesized that MT molecules act as sacrificial targets, sparing critical cellular macromolecules from damage by reactive cytotoxic agents. MT may protect normal tissues from damage, or its expression in cancer cells may contribute to cellular drug resistance in tumors. We have observed that cisplatinum or radiation, which are unable to induce MT expression in cultured cells, can induce organ-specific MT expression in mouse tissues.[1-3] We are studying the possible role of MT in mediating cellular drug and radiation resistance by transfecting mouse and human MT genes, under the control of promoters that allow expression of MT in the absence of induction by a toxic heavy metal, into recipient mouse-lymphoma or CHO cells. We are using the resulting chimeric cells to study cellular drug and radiation resistance without the complicating nonspecific effects of toxic metal induction of MT expression. Parallel studies are underway to measure constitutive and therapy-induced MT expression in human ovarian and cervical carcinomas.

This project is supported by grants from the Medical Research Council of Canada, and the Victoria Hospital Research Development Fund.

REFERENCES

1. Koropatnick J, Cherian MG: Exposure to different forms of cadmium in mice: Differences in metallothionein and alfafetoprotein mRNA induction in liver and kidney. J Biochem Toxicol 1988; 3: 159.
2. Singh G, Koropatnick J: Differential toxicity of cis and transisomers of dischlorodiammineplatinum. J Biochem Toxicol 1988; 3: 223.
3. Koropatnick J, Leibbrandt MEI, Cherian MG: Organ-specific metallothionein induction in mice by x-irradiation. Radiat Res 1989; 119: 356.

---

*CS-103-1.

**Career Scientist, OCTRF London Regional Cancer Centre; and Assistant Professor of Oncology, and of Microbiology and Immunology, University of Western Ontario, London.

†Professor of Pathology, UWO.

††Assistant Professor of Pediatrics, UWO.

PREPARATION OF MONOCLONAL ANTIBODIES AGAINST METALLOTHIONEIN*

J. KOROPATNICK** and J.F. HARRIS†, *London, Ontario*

Metallothioneins (MTs) are small, cysteine-rich proteins, which are present in most species of the plant and animal kingdoms. Earlier work has suggested that they play a role in detoxification of heavy metals, metal homeostasis and in resistance to reactive toxic agents and radiation. In humans and animals increased expression of MTs indicates exposure to heavy metals. In view of their potential use as markers of exposure to toxic molecules and mediators of resistance, we require a sensitive and specific immunological detection assay. Previous attempts to facilitate such assays by production of monoclonal antibodies directed against specific human or rodent MTs have met with little or no success, presumably because of the widespread presence and immunosuppressive qualities of the MT protein in most mammals. We are using MT cDNA constructs in a bacterial protein expression system to produce protein fragments of both human and mouse MTs for use as immunogens to elicit an immune response in mice. This approach will be used: a) to diminish or eliminate the immunosuppressive effect of non-immunogenic portions of the protein; b) to identify and map the antigenic regions; and c) to produce immunogenic "mini proteins" which will stimulate production of antibodies capable of distinguishing MT from other metal-binding proteins.

This project is supported by a grant from the Victoria Hospital Research Development Fund.

---

* CS-103-2.

** Career Scientist, OCTRF London Regional Cancer Centre; and Assistant Professor of Oncology, and of Microbiology and Immunology, University of Western Ontario, London.

† Career Scientist, OCTRF London Regional Cancer Centre; and Assistant Professor of Oncology, and of Microbiology and Immunology, UWO.

SOMATIC CELL GENETIC ANALYSIS OF METASTATIC CELLS*

J.F. HARRIS** and A.F. CHAMBERS†, *London, Ontario*

Oncogenes are implicated in human malignancy but their precise mechanisms of action remain poorly understood. Recently, NIH 3T3 cells transformed with a variety of *ras* oncogenes, including H-, K-, and N-, of viral or cellular origin, have been shown to have increased resistance to ionizing radiation[1]. The increased resistance of the transformed cells (as compared with normal NIH 3T3 cells) was related to an increase in D_0, the parameter representing the inverse slope of the single-dose, radiation survival curve. Increased resistance to radiation was seen in both morphologically transformed cells and revertant *ras* transfected lines, which were no longer transformed. In another study of NIH 3T3 cells, the human N-*ras* oncogene enhanced x-irradiation survival at high dose rates (200 cGy/min) but not at low dose rates 5 cGy/min)[2].

Members of the *ras* family of genes are involved in the malignant transformation of several common human neoplasms including lung cancer, breast cancer and myeloid leukemia[3]. Thus the effects of *ras* oncogenes on radiation survival of cancer cells is an important clinical issue, especially for tumors treated with radiotherapy.

We examined the effect of ^{60}Co-irradiation on the clonogenic survival of rat NRK cells, NRK cells carrying a temperature-sensitive viral K-*ras* oncogene (tsK-NRK), mouse NIH 3T3 cells and NIH 3T3 cells transformed with the human bladder cancer (T24) H-*ras* oncogene (PAP2)[4]. We tested the hypothesis that *ras* oncogene expression renders cells more resistant to radiation but found in both systems that *ras*-transformed cells were more, not less, sensitive to radiation. We also found indications of altered repair of sublethal radiation damage. PAP2 cells were more sensitive to radiation than NIH 3T3 cells. Increased sensitivity was reflected in a decreased shoulder region of the survival curve with little effect on its slope(D_0). TsK-NRK cells also were slightly more sensitive to radiation than NRK and exhibited decreased repair of sublethal damage at both the permissive and non-permissive temperatures. Thus, we found that expression of *ras* oncogenes is not always associated with increased radiation resistance.

In summary, our results suggest that (a) in some cells, *ras* oncogene may be associated with increased, rather than decreased, radiation sensitivity and (b) *ras* oncogene expression may alter the shoulder region of the dose-response curve, suggesting changes in the repair of sublethal radiation damage.

This project is supported by a grant from the Medical Research Council of Canada.

---

* CS-150-2.

** Career Scientist, OCTRF London Regional Cancer Centre:: and Assistant Professor of Oncology and of Microbiology and Immunology, University of Western Ontario, London.

† Career Scientist, OCTRF London Regional Cancer Centre: and Associate Professor of Oncology, and of Microbiology and Immunology, UWO.

REFERENCES

1. Sklar MD: The *ras* oncogenes increase the intrinsic resistance of NIH 3T3 cells to ionizing radiation. *Science* 1988; **239:** 645.
2. FitzGerald TJ, Daugherty C, Kase K, Rothstein LA, McKenna M, Greenberger JS: Activated human N-*ras* oncogene enhances x-irradiation repair of mammalian cells in vitro less effectively at low dose rate. *Am J Clin Oncol* 1985; **8:** 517.
3. Chambers AF, Tuck AB: Oncogene transformation and the metastatic phenotype. *Anticancer Res* 1988; **8:** 861.
4. Harris JF, Chambers AF, Tam ASK: Some *ras*-transformed cells have increased radiosensitivity and decreased repair of sublethal radiation damage. *Somat Cell Mol Genet* 1990; **16**: 39.

CONTRIBUTION OF ONCOGENES TO TUMOR METASTASIS*

A.F. CHAMBERS**, *London, Ontario*

Oncogene transfection is a useful tool in analyzing the mechanisms of tumor metastasis[1]. We have shown that transfection of NIH 3T3 cells with the T24 H-*ras* oncogene can convert these cells to a metastatic phenotype[2]. The *ras*-transformed cells can be selected in vivo for increased metastatic ability in chick embryos and the selected cell populations express increased levels of *ras* p21 protein[3]. We have shown that metastatic ability of these cells is directly related to their levels of *ras* expression[3]. We hypothesize that metastatic ability in these cells is due to expression of *ras*-induced genes, which contribute more directly to metastasis. One such gene may be a transformation-related, secreted phosphoprotein (sppl/osteopontin), which is expressed at high levels in metastatic, *ras*-transformed NIH 3T3 cells[4].

Recently we tested the metastatic properties of a series of these cells in nude mice to determine if metastatic ability in the chick embryo assay predicts metastatic behavior in nude mice. We have found that cells selected for metastatic ability in the chick embryo are also metastatic when assayed in nude mice. Using an immunocytochemical procedure, we also found heterogeneity in p21 expression among individual cells in these populations, with the proportions of p21-expressing cells increasing in cells selected for metastatic ability. These results suggest that the metastasis assay in the chick embryo[5] offers an efficient and cost-effective procedure for seletion of cells that also are metastatic in nude mice, and that the metastatic ability of *ras*-transformed NIH 3T3 cell lines is due to individual cells that express increased amounts of p21 protein.

To extend our studies on the role of *ras* in metastasis, we have examined the effect of the H-*ras* oncogene on another cell line, tumorigenic but non-metastatic murine LTA cells. These cells did not become metastatic (when tested in chick embryos or nude mice) even when expressing high levels of p21. This finding suggests that high levels of *ras* expression do not always result in the induction of metastatic ability. This cell line offers an opportunity to study natural mechanisms of resistance to *ras*-induced metastasis.

This research is supported by a grant from the National Cancer Institute of Canada.

---

* CS-150-3.

** Career Scientist, OCTRF London Regional Cancer Centre; and Associate Professor of Oncology, and Microbiology and Immunology, University of Western Ontario, London.

REFERENCES

1. Chambers AF, Tuck AB: Oncogene transformation and the metastatic phenotype. *Anticancer Res* 1988; **8:** 861.
2. Bondy GP, Wilson S, Chambers AF: Experimental metastatic ability of H-*ras*-transformed NIH3T3 cells. *Cancer Res* 1985; **45:** 6005.
3. Hill SA, Wilson S, Chambers AF: Clonal heterogeneity, experimental metastatic ability, and p21 expression in H-*ras*-transformed NIH 3T3 cells. *J Natl Cancer Inst* 1988; **80:** 484.
4. Craig AM, Nemir M, Mukherjee BB, Chambers AF, Denhardt DT: Identification of the major phosphoprotein secreted by many rodent cell lines as 2ar/osteopontin: Enhanced expression in H-*ras*-transformed 3T3 cells. *Biochem Biophys Res Commun* 1988; **157:** 166.
5. Chambers AF: Use of the chick embryo in studying the molecular genetics of metastasis. *In:* Lapis K, Liotta LA, Rabson AS, eds. Biochemistry and Molecular Genetics of Cancer Metastasis. Boston: Martinus Nijhoff Publishing, 1986: 11.

STABILITY OF HUMAN MONOCLONAL ANTIBODY PRODUCTION IN MOUSE-HUMAN HYBRIDOMA CELLS*

J. KOROPATNICK** and J.F HARRIS†, *London, Ontario*

New developments in mouse monoclonal antibodies have increased their usefulness as biological probes and potential therapeutic agents. However, the instability of human monoclonal antibody production by mouse-human hybridoma cells (and the lack of a human fusion partner that does not secrete immunoglobulins) keeps us from extending this technology to human immunoglobulins. However, in some clones at least, one mouse myeloma parent line (SHM-D33) has proved to be as stable for human antibody as mouse hybridoma cells are for mouse antibody[1]. Analysis of a panel of these hybridomas[2] has shown that: 1) there is a close correlation between loss of structural human antibody genes and loss of human antibody production; 2) there is considerable heterogeneity for human DNA content among antibody-positive cells; and 3) loss of antibody production is accompanied by large losses of human, but not mouse, DNA. Human DNA continued to be lost at a high rate after antibody production ceased.

In continuing these studies, we have followed the stability of a human IgM-producing hybridoma (E10) from its initial isolation to its growth to large population size. To follow the stability of IgM production, we have developed a rapid immunochemical procedure for the analysis of the frequency of IgM-producing cells in situ, from hybridoma colonies. Using this assay, a higher frequency of IgM-non-secreting E10 cells was observed shortly after the isolation of E10 relative to clonal derivatives of E10. Thus, more stable IgM-producing cells were obtained following repeated cloning. In addition, ionizing radiation was effective in destabilizing E10 cells because the frequency of IgM-non-producing clones was increased significantly after irradiation (400-600 cGy). Although the total DNA content of E10 cells did not change following irradiation, the human DNA content of E10-irradiated cells, both IgM-producers and IgM-non-producers, was reduced significantly. These results, which support our finding that the human DNA content of heteromyeloma cells is variable in individual clones2, suggest that human DNA is repaired less effectively following DNA damage by ionizing radiation. The in situ immunochemical staining for human antibody production is a valuable addition to the monitoring of total secreted IgM to evaluate nascent hybridoma cells for their stability of antibody production.

This project was supported by a grant from the Cancer Research Society, Inc.

---

* CS-151-1.

** Career Scientist, OCTRF London Regional Cancer Centre; and Assistant Professor of Oncology, and Microbiology and Immunology, University of Western Ontario, London.

† Career Scientist, OCTRF London Regional Cancer Centre; and Assistant Professor of Oncology, and Microbiology and Immunology, UWO.

REFERENCES

1. Gardner JS, Chiu ALH, Maki NE, Harris JF: A quantitative stability analysis of human monoclonal antibody production by heteromyeloma hybridomas, using an immunofluorescent technique. *J Immunol Methods* 1985; **85:** 334.
2. Koropatnick J, Pearson J, Harris JF: Extensive loss of human DNA accompanies loss of antibody production in heteromyeloma hybridoma cells. *Mol Biol Med* 1988; **5:** 69.

DEVELOPMENT AND CHARACTERIZATION OF MONOCLONAL ANTIBODIES TO METASTATIC TUMOR CELLS*

J.F. HARRIS**, *London, Ontario*

We have proposed a "dynamic heterogeneity model" in which a subpopulation of specialized, highly metastatic cells are generated and lost during clonal expansion[1-4]. This model was used to devise a screening procedure for monoclonal antibodies (MAb) based on the differential immunochemical staining of cell populations differing in metastatic ability. Embryonal carcinoma cells, which recently were derived from a liver metastasis4, were used to immunize mice against a variety of developmental antigens, some of which may be relevant to the metastatic phenotype. The resulting MAb were screened using a sensitive immunochemical staining technique against highly metastatic (KHT35-L1)3 and weakly metastatic (KHTp) fibrosarcoma cells. In this way, one of the MAb, SG-1, was chosen for further study because of its preferential binding to KHT35-L1 cells.

Quantitative absorption, binding and in situ immunochemical staining assays indicate that the MAb SG-1-defined epitopes are expressed preferentially by the highly metastatic KHT35-L1 cells relative to the weakly metastatic KHTp cells. MAb SG-1 binding to antigen was inhibited by specific sulfated polysaccharides including cerebroside sulfate (brain sulfatide) and dextran sulfate (500 kD) but not in heparan, chrondroitin, keratan or dextran (5 kD) sulfates. Initial characterization of antigen from KHT cells indicates that the epitope of MAb SG-1 is defined by sulfated glycoconjugates containing galactose and sulfate. The antigen partitions in total lipid extracts of KHT35-L1 cells as both delipidated protein and as chloroform/methanol-soluble glycoprotein or glycolipid.

Following trypsin treatment, there was a significant correlation ($p<0.05$) between the expression of MAb SG-1-defined antigen on the cells and their metastatic ability. These results suggest that the sulfated glycoconjugate determinants identified by MAb SG-1 may be relevant to the metastatic process of KHT fibrosarcoma cells.

This project is supported by grants from the Medical Research Council of Canada, and the Victoria Hospital Research Development Fund.

---

* CS-151-3.

** Career Scientist, OCTRF London Regional Cancer Centre; and Assistant Professor of Oncology, and Microbiology and Immunology, University of Western Ontario, London.

REFERENCES

1. Harris JF, Chambers AF, Hill RP, Ling V: Metastatic variants are generated spontaneously at a high rate in mouse KHT tumor. *Proc Natl Acad USA* 1982: **79:** 5547.
2. Chambers AF, Harris JF, Ling V, Hill RP: Rapid phenotype variation in cells derived from lung metastases of KHT fibrosarcoma. *Invasion Metastasis* 1984: **4:** 225.
3. Harris JF, Chambers AF, Ling V, Hill RP: Dynamic heterogeneity: Characterization of two cell lines derived from experimental lung metastases of mouse KHT fibrosarcoma. *Invasion Metastasis* 1987: **7:** 217.
4. Harris JF, Best MW: Dynamic heterogeneity: Metastatic variants to liver are generated spontaneously in mouse embryonal carcinoma cells. *Clin Exp Metastasis* 1988: **6:** 451.

STRUCTURE/FUNCTION AND HORMONAL REGULATION OF PLASMA STEROID BINDING PROTEINS*

G.L. HAMMOND**, *London, Ontario*

Two high-affinity, steroid-binding proteins —corticosteroid-binding globulin (CBG) and sex-hormone-binding globulin (SHBG) are found in the blood of most mammalian species. A major function of these proteins is transport but they also regulate steroid bioavailability and may participate in the delivery of steroids to specific target cells[1].

A variety of malignant tumors are steroid-hormone dependent but no one has shown how they induce tumor formation. Because CBG and SHBG modulate steroid bioavailability, we have focussed on studies of the structure, function and biosynthesis of these proteins[2-5]. We discovered that CBG is a member of the serine, protease-inhibitor-gene family and demonstrated that this protein is a specific substrate for neutrophil elastase. As a result of this interaction, cortisol is released to neutrophils during the inflammatory process and this fact may explain in large part the anti-inflammatory properties of glucocorticoids.

Recently we isolated and characterized the human genes for both SHBG[6] and CBG[7] and are using these cloned genes to identify factors responsible for their tissue specificity with respect to expression and hormonal regulation. By phylogenetic comparisons of the primary structures of CBG and SHBG, we have demonstrated conserved regions which may have biological importance. We are in the process of identifying point mutations which appear to be responsible for variant proteins that demonstrate abnormal steroid binding activity. We are using the information derived from these studies to create structural mutants of SHBG and CBG by site-directed mutagenesis; this work should help to define the functional properties of these proteins at a molecular level. We anticipate that the results of these studies will help us understand more clearly the mechanisms through which steroids interact with binding proteins and with target cells. Thereby we hope to gain insight into the etiology and possible control of hormone-dependent cancers.

These projects are funded by the Medical Research Council of Canada, and the Ontario Thoracic Society.

---

* RS-230.

** OCTRF Research Scholar; Director, Cancer Research Laboratories, London Regional Cancer Centre; and Associate Professor of Obstetrics and Gynecology and Oncology, University of Western Ontario, London.

REFERENCES

1. Siiteri PK, Murai JT, Hammond GL, Nisker JA, Raymoure WJ, Kuhn RW: The serum transport of steroid hormones. *Recent Prog Horm Res* 1982: **38:** 457
2. Hammond GL, Smith CL, Goping IS, Underhill DA, Harley MJ, Reventos J, Musto NA, Gunsalus GL, Bardin CW: Primary structure of human corticosteroid binding globulin deduced from hepatic and pulmonary cDNAs exhibits homology with serine protease inhibitors. *Proc Natl Acad Sci USA* 1987; **84:** 5153.
3. Hammond GL, Underhill DA, Smith CL, Goping IS, Harley MJ, Musto NA, Cheng CY, Bardin CW: The cDNA-deduced primary structure of human sex hormone binding globulin and location of its steroid binding domain. *FEBS Lett* 1987; **215:** 100.
4. Smith CL, Hammond GL: Rat corticosteroid binding globulin: primary structure and mRNA levels in the liver under different physiological conditions. *Mol Endocrinol* 1989; **3:** 420.
5. Seralini G-E, Underhill CM, Smith CL, Nguyen V, Hammond GL: Biological half-life and transfer of maternal corticosteroid binding globulin (CBG) to amniotic fluid in the rabbit. *Endocrinology* 1989; **125:** 1321.
6. Hammond GL, Underhill DA, Rykse HM, Smith CL: The human sex hormone binding globulin gene contains exons for androgen binding protein and two other testicular messenger RNAs. *Mol Endocrinol* 1989; **3**: 1869.
7. Underhill DA, Hammond GL: Organization of the human corticosteroid binding globulin gene and analysis of its 5' flanking region. *Mol Endocrinol* 1989; **3:** 1448.

ADDITIONAL INVESTIGATIONS

Dr. L. Levin, Chief Executive Officer LRCC and Vice-President OCTRF, reports on the following clinical research investigations:

MELANOMA AND RENAL-CELL CANCER

Investigators: V. Bramwell and W. Mertens
This is a co-ordinated study of the use of interleukin-2 and indomethacin in advanced melanoma and renal-cell cancer. Funding comes from the NCI and NCIC grants.

SARCOMA

Investigator: V. Bramwell
Dr. Bramwell is the national co-ordinator/chairperson for the Canadian Sarcoma Group that collaborates with the EORTC on clinical studies. This group is partly funded by the NCIC. We now have a data base for all sarcomas that have been presented to the London Centre since 1984.

AUTOLOGOUS BONE MARROW REINFUSION (TRANSPLANTATION)

Investigator: A. Smith
Recent evidence suggests that high-dose chemotherapy supported by autologous bone marrow reinfusion can produce prolonged disease-free survival in 20 to 25% of patients with diffuse, large-cell lymphoma or Hodgkin's disease refractory to standard chemotherapy and radiotherapy. Bone marrow is being harvested in the London Centre's operating suite. This program will enable the Centre to participate in clinical research protocols, which evaluate dose intensity in a variety of tumors.

MYELOPROLIFERATIVE DISEASES

The London Centre is participating in a number of protocols which explore the use of GM-CSF or IFN in the myeloproliferative diseases. A lymphoma data base provides information about prognostic factors and permits us to audit the results of treatment in Hodgkin's disease and non-Hodgkin's lymphomas.

OVARIAN CANCER

Investigators: L. Levin and J. Rusthoven
This phase I study assess the use of high-dose carboplatinum and cyclophosphamide, in association with the biological response modifier GM-CSF as a myeloprotective agent.

COLORECTAL CANCER

Investigator: J. Skillings

An ad hoc OCTRF committee, chaired by Dr. Skillings, is examining the usefulness of 5-FU and levamisole in Duke's Stage C colorectal cancer, and will develop a protocol for the administration of 5-FU and IFN in metastatic disease.

PROSTATIC CANCER

Investigators: A. Porter and J. Battista

The London Centre is at the forefront of clinical research in brachytherapy for prostatic cancer. In collaboration with the Division of Nuclear Medicine, Victoria Hospital, it is the national co-ordinating centre for strontium studies in prostatic cancer.

BREAST CANCER

Investigators: L. Levin and D. Goettler

Breast has shown a strong relationship to diet. These investigators will study the influence of dietary fat on hormone release in post-treatment breast cancer, in collaboration with the Department of Biochemistry, University of Western Ontario, and the Gastrointestinal Centre at Genessee Hospital in Rochester, N.Y. London Centre is also a major contributor to a pilot study in Stage II breast cancer, which is exploring dose escalation of a combination of 5-FU, epirubicin and cyclophosphamide. Dr. V. Bramwell is a member of the writing committee for MA-5, a follow-up Phase III NCIC study.

LUNG CANCER

Investigators: L. Levin and D. Goettler

In collaboration with the Departments of Surgery and Pathology, Victoria Hospital, these workers are investigating the relationship between Vitamin A, cell differentiation and proliferation rates in lung cancer.

BRAIN TUMOR STUDIES

The principal research focus of the neuro-oncology group at the London Centre continues to be the treatment of malignant brain tumors in adults. The group contributes to clinical trials of newly diagnosed and recurrent malignant glioma (CNS Cancer Consortium), newly diagnosed and recurrent anaplastic oligodendroglioma (NCIC), primary CNS lymphoma (RTOG), low-grade glioma (BTCG/RTOG/SWOG) and solitary brain metastasis (OCOG). Studies continue of steroid-induced MRI changes in patients with recurrent malignant glioma, studies of cognitive function in successfully treated brain-tumor patients and selected retrospective reviews. Laboratory interests include experimental glioma metastasis and basic mechanics of radioresistance and chemoresistance in glial tumors.

Ottawa Regional Cancer Centre

MECHANISM OF OXYGEN-RADICAL DAMAGE TO CELLULAR DNA AND ITS ROLE IN TUMOR PROMOTION AND TUMOR PROGRESSION*

H.C BIRNBOIM**, *Ottawa, Ontario*

"Professional" phagocytes such as granulocytes, monocytes and macrophages produce superoxide anion (0_2^-) in response to a variety of particulate and soluble stimuli such as the tumor promoter, phorbol myristate acetate (PMA). A multicomponent "respiratory burst oxidase", which uses NADPH to reduce bimolecular oxygen 0_2, has been partially characterized; it is the source of 0_2^-. In turn, 0_2^- can generate H_20_2. These oxyradicals likely are produced *in situ* by phagocytic cells frequently present in inflammatory extracts and in solid tumors. We have shown that these oxyradicals can cause DNA strand breaks in the "effector" cell and in nearby "target" cells. We postulate that the strand breaks in target cells can contribute to the "promotion" and "progression" stages of cancer by causing genomic alterations such as translocations, rearrangements and amplifications detected at the chromosome or the genomic level. Such alterations may activate a second oncogene in an early tumor cell (in which one ocogene has already been activated as a result of exposure to a carcinogen), causing it to progress to a more malignant phenotype. Alternatively, they may inactivate tumor suppressor genes, such as the product of the retinoblastoma locus.

We have continued our studies into the mechanism of DNA strand breakage by 0_2^- in PMA stimulated human granulocytes. While many laboratories have shown that H_20_2 can produce DNA breaks in intact cells, our laboratory has developed the granulocyte as a model system for demonstrating that 0_2^- also can cause breaks. In essentially no other system has it been shown that 0_2^- can do this. Because of the potential importance of these reactions to cancer progression, we have continued to focus on the mechanisms involved. Recently, we developed a method for isolating pure human granulocytes in 100% yield. To this point, most of our work was done with a mixed leukocyte population (80-85% granulocytes) because the amount of blood obtainable from volunteers is limited and the number of cells required is large. With pure granulocytes, we have been able to present even more convincing evidence that 0_2^- causes breaks independent of H_20_2. Although the cells produce large amounts of H_20_2, catalase, an enzyme which removes H_20_2, had virtually no effect on the yield of strand breaks. We attribute this to the fact that granulocytes have high levels of intracellular catalase. In mixed leukocyte preparations, DNA in lymphocytes is a target for H_20_2 because these cells have very low levels of catalase; therefore, catalase added to the medium can protect their DNA from H_20_2 produced by granulocytes.

---

* CS-104-2.

** Career Scientist, and Head of Experimental Oncology, OCTRF Ottawa Regional Cancer Centre, General Division; and Professor of Medicine, of Microbiology and Immunology, and of Biochemistry, University of Ottawa.

Addition of superoxide dismutase (SOD) does not protect either the DNA of pure granulocytes of that of mixed leukocytes, even though most or all of the 0_2^- is produced extracellularly. The explanation for the apparent paradox may be that exogenous SOD cannot access the site at which 0_2^- produces its initial effect, which may be at the external cytoplasmic membrane surface or within the membrane. Our earlier studies showed that activation of the respiratory burst to produce 0_2^- is needed to induce breaks, that only a small amount of 0_2^- is needed to initiate breaks and that metabolic inhibitors such as sodium fluoride can block break production. Since a membrane site might not be accessible to added native SOD because of its charge, we prepared "lipophilic" SODs with fatty-acid chains (laurate, myristate, palmitate) attached to lysine residues. None of these moieties were able to block strand breakage. However, small molecules, which react rapidly with 0_2^-, were very effective. A charged catechol compound – 3,4-dihydroxybenzoate – blocked breaks at concentrations of 0.25-0.5 mM. Uncharged catechol compounds were even more potent: 0.5-2.0 micromolar catechol, gossypol, urushiol blocked >80% of breaks. Similar low concentrations of diethystilbestrol and benzoquinone were equally effective. This and other evidence supports the notion that a cytoplasmic membrane target for 0_2^- activates a transmembrane signal to produce strand breaks in nuclear DNA.

This project is supported by a grant from the Medical Research Council of Canada.

SITES OF DNA STRAND BREAKS IN PMA-STIMULATED HUMAN GRANULOCYTES[*]

H.C BIRNBOIM[**], *Ottawa, Ontario*

As described earlier (CS-104-2), stimulation of human granulocytes with phorbol ester (PMA) induces a "burst" of oxyradicals, which soon is followed by a "burst" of DNA breaks. If 0_2^- activates a specific DNA strand break mechanism it is possible that the breaks are induced at specific sites in the genome. If 0_2^- activates a non-specific mechanism, such as the release of reactive lipid species from the membrane, one might expect the breaks at random sites in the genome. To test these alternative possibilities, we have devised a new method to look at genes located at the DNA breakpoints. If breaks are introduced randomly, then all genes should be represented at the breakpoints. Conversely, if breaks are induced at specific sites, some genes should be found preferentially at breakpoints. To study genes in the vicinity of breakpoints, DNA is labelled as follows. After DNA breaks are induced with PMA, whole cells are embedded in agarose beads. Cells are subjected to limited treatment with alkali so that only a fraction of the duplex DNA is unwound – in the vicinity of the breakpoints. The single-stranded DNA at the breakpoint is labelled using the oligonucleotide-primed method with ^{32}P-dCTP. Then this labelled DNA is used to probe a battery of different (cloned) genes, immobilized on a membrane. Our early results with this method appear to show that some genes are indeed preferentially labelled. However, specific involvement of 0_2^- has not yet been demonstrated.

This project is supported by a grant from the Medical Research Council of Canada.

---

[*] CS-104-3.

[**] Career Scientist, and Head of Experimental Oncology, OCTRF Ottawa Regional Cancer Centre; and Professor of Medicine, of Microbiology and Immunology, and of Biochemistry, University of Ottawa.

IN VITRO AND IN VIVO INDUCTION BY GRANULOCYTE-DERIVED OXYRADICALS OF MUTANTS AT THE HPRT LOCUS IN MOUSE CELLS*

H.C. BIRNBOIM**, *Ottawa, Ontario*

The hypoxanthine phosphoribosyltransferase (HPRT) gene is X-linked and is present in a single copy in normal male cells. This gene is particularly useful in the study of genomic alterations, such as mutations and deletions, because we have powerful selection methods that allow us to discriminate between cells which either lack or contain a functional gene. Cells which lack a functional gene product resist completely the cytotoxic effects of a guanine analogue, 6-thioguanine (TG). Conversely, cells which contain an active gene product resist aminopterin in the presence of hypoxanthine and thymidine ('HAT' medium). In earlier studies, we had established cell lines from a transplantable mouse fibrosarcoma line, Mc1A[1]. The tumor originated from a male animal. In the present study, we are using these lines to establish a model system for studying the induction of mutants at the HPRT locus by oxyradicals in vitro as well as in vivo. We will use the in vivo system to test the hypothesis that phagocytic cell, such as granulocytes and macrophages, within solid tumors are a source of genotoxic oxyradicals that have the potential to produce large genomic alterations.

For reasons not yet established, in these cells it has proved difficult to induce HPRT$^-$ mutants by various sources of oxyradicals, by ionizing radiation or even by powerful mutagens such as methyl nitrosourea. There is no indication that there are two copies of the X-chromosome in the cell. As have others, we propose that mutational studies with X-linked genes may be more difficult because loss of the gene may be accompanied by loss of other X-linked genes essential for cell viability. To circumvent these problems, we have attempted to inactivate the X-linked gene and introduce another HPRT gene on an autosome so that if loss of the introduced HPRT gene was accompanied by loss of adjacent essential genes, the cell would still be viable because a second copy of the essential gene was present on the second chromosome. After considerable difficulty, we isolated some HPRT$^-$ variants, i.e., resistant to TG, and tested these for the stability of their TG^r phenotype. Among these, we identified some clones which appear to have deleted the gene, i.e., the reversion frequency was very low (<1 in 10^7). The cell lines are still capable of forming subcutaneous tumors in syngeneic animals. Into several of these clones, a human HPRT minigene (obtained from Dr. P. Patel) was transfected by electroporation. Currently we are selecting cells resistant to HAT medium. It is anticipated that the cell lines we are developing will prove to be a useful quantitative model system with which to study, phenotypically and molecularly, genomic alterations induced at the HPRT locus by oxyradicals.

This project is supported by a grant from the National Cancer Institute of Canada.

---

*CS-104-4.

**Career Scientist, and Head of Experimental Oncology, OCTRF Ottawa Regional Cancer Centre; Professor of Microbiology and Immunology and of Biochemistry, University of Ottawa.

REFERENCE

1. Kadhim S, Burns BF, Birnboim HC: In vivo induction of tumor variants by phorbol 12-myristate 13-acetate. *Cancer Lett* 1987; **38:** 209.

ALTERATIONS IN METHIONINE METABOLISM ASSOCIATED WITH TUMOR PROGRESSION*

R.G. LITEPLO**, *Ottawa, Ontario*

A major focus in cancer biology involves the identification of those biochemical, cellular and molecular mechanisms which are responsible for the autonomous growth of tumor cells and which are associated with, or contribute to, the "malignant phenotype". Our laboratory has been studying the role of intracellular transmethylating activities and aspects of methionine metabolism in human tumor cells of varying malignant potential to determine how such metabolic changes are associated with the progression of human tumors from relatively benign to highly malignant and autonomous states.

Normal cells (as well as some human tumor cells) can grow in culture medium devoid of exogenous methionine but containing its immediate precursor, homocysteine. In contrast, most human tumor-cell lines exhibit a reduced ability to grow in such methionine-free, homocysteine-supplemented culture medium. We have proposed that the terms "homocysteine-responsive" and "homocysteine-nonresponsive" be used to describe cells which either can or cannot grow in methionine-free, homocysteine-supplemented culture medium, respectively. We have found that a series of highly metastatic, variant cell lines, which had been derived from a poorly-metastatic (homocysteine-responsive) human melanoma tumor line, exhibit a homocysteine-nonresponsive phenotype. In a separate study, we found that the majority of cell clones which were isolated from either a (homocysteine-responsive) human melanoma or neuroepithelioma cell line on the basis of their enhanced ability to proliferate in an anchorage-independent manner, also exhibit this homocysteine-nonresponsive phenotype. Homocysteine-responsive revertants isolated from a homocysteine-nonresponsive, human melanoma cell line exhibit a diminished growth rate and reduced ability to proliferate in an anchorage-independent manner. The failure of these homocysteine-nonresponsive variants to proliferate in methionine-free, homocysteine-supplimented medium appears to be due to a deficiency in the synthesis of methionine from homocysteine and 5-methyltetrahydrofolic acid, which also may be associated with a reduction in the methylation of cobalamin. These observations suggest that alterations in methionine metabolism (possibly arising from changes in certain transmethylating activities) are associated with the evolution of human tumors from relatively benign to highly malignant and autonomous states. These alterations in methionine metabolism could provide a basis for the development of new therapeutic strategies aimed at the selective elimination of the most aggressive or malignant cells within a developing tumor.

This project is supported by a grant from the National Cancer Institute of Canada.

---

[*] CS-108-2.

[**] Career Scientist, OCTRF Ottawa Regional Cancer Centre; and Assistant Professor of Medicine and Biochemistry, University of Ottawa.

SIGNAL TRANSDUCTION PROCESSES ASSOCIATED WITH THE MITOGENIC RESPONSE*

R.G. LITEPLO**, *Ottawa, Ontario*

There is a great deal of interest in cancer biology in elucidating the mechanisms by which cells respond to extracellular growth stimuli and how such pathways are altered in tumor cells. Concerning the identification of those pathways associated with the cell's response to an extracellular stimulus much effort is being expended to elucidate the biochemical and molecular signals which regulate or modulate the ability of quiescent cells to enter a proliferative state.

We have proposed that the carboxymethylation of cellular proteins is one of the post-translational modification reactions involved in the signal transduction process associated with the mitogenic response of quiescent cells to growth factor stimulation. Alterations in the carboxymethylation of specific proteins may influence their enzymatic activity or function, such as the capacity to interact with other proteins or biological macromolecules, including DNA. This covalent modification of nuclear transcription factors could alter the expression of genes which play a role in the regulation of DNA synthesis and cell proliferation.

After quiescent rodent cells are exposed to mitogenic growth factors, the effect on total cellular protein carboxymethylation, protein carboxymethyltransferase activity, the carboxymethylation of nuclear transcription factors as well as the metabolic turnover of carboxymethyl-groups on cellular proteins are being determined. Other studies will seek to elucidate which biochemical pathways regulate protein carboxymethylation in eukaryotic cells. Initial observations indicate that, when quiescent cells are stimulated to proliferate, total cellular protein carboxymethylation increases before the onset of DNA synthesis.

The long-term goal of this project is to determine the role of this post-translational modification in modulating the transcriptional activity of the specific genes involved in the control of cell proliferation. Such information could provide a basis for the development of new therapeutic strategies aimed at stopping the uncontrolled growth of cancer cells.

This project is supported by a grant from the National Cancer Institute of Canada.

---

* CS-108-5.

** Career Scientist, OCTRF Ottawa Regional Cancer Centre; and Assistant Professor of Medicine and Biochemistry, University of Ottawa.

ROLE OF INTERLEUKIN-6 IN B-CELL NEOPLASIA

R.G. HAWLEY**, Ottawa, Ontario

Interleukin-6 (IL-6), a glycoprotein of 26 kDa produced predominantly by monocytes and macrophages, exhibits pleiotropic activities on a wide variety of cells. In particular, IL-6 is a potent growth factor for mouse plasmacytoma/hybridoma cells and human myelomas.

We are using an IL-6-dependent, mouse B-cell hybridoma (B9) as a model system to investigate the mechanism of IL-6-induced cellular proliferation. B9 cells die within 72 hours after IL-6 is removed from the growth medium. Cell-cycle analysis 48 hours after IL-6 removal indicates that, before cell death, the majority of B9 cells arrest in the G1 phase of the cycle. When IL-6 is added at this time, B9 cells will proceed through G1 and enter S phase about 10 to 12 hours later. There are no changes in the steady-state levels of the "competence" genes that, during this 10- to 12-hour period, are induced transiently in quiescent fibroblasts shortly after serum stimulation. To identify genes, which exhibit enhanced transcription or enhanced mRNA stabilization during the IL-6-induced proliferation of G1-arrested B9 cells, we are screening by differential hybridization a cDNA library enriched in mRNA sequences at the 10-hour time point. By isolating cDNAs of genes whose expression is coupled to entry into S phase, we hope to identify the genes which play a regulatory role in IL-6-induced cell proliferation.

Because autocrine production of IL-6 has been reported in human myeloma, we introduced the human IL-6 gene into B9 cells by retrovirally-mediated gene transfer to determine the role that constitutive Il-6 gene expression might play in tumor progression and/or metastasis. Growth factor-autonomous cells were shown to secrete biologically-active hIL-6. The tumorigenicity of the IL-6-independent cells and their ability to yield experimental metastases were evaluated by subcutaneous and intravenous injection, respectively, into syngeneic and athymic (nude) mice. All cell lines gave rise to progressively growing tumors at the sites of subcutaneous injection and two to three months after intravenous injection rare metastases were found in the bone marrow and ovaries of mice. Unexpectedly, a similar outcome was obtained with the parental B9 cells. Moreover, we found that B9-derived tumor cells still required IL-6 for their growth in vitro. These results indicate that mice produce sufficient IL-6 to support the growth of the IL-6-dependent cells and that autocrine production of IL-6 does not enhance the tumorigenicity or the metastatic capacity of these cells.

These projects are supported by grants from the National Cancer Institute of Canada and The Arthritis Society.

---

* CS-110.

** Career Scientist, OCTRF Ottawa Regional Cancer Centre; and Assistant Professor of Medicine, and Microbiology and Immunology, University of Ottawa.

REGULATION OF HEMATOPOIESIS BY INTERLEUKIN-1α*

R.G. HAWLEY**, *Ottawa, Ontario*

In 1986, it was first reported that a factor purified from the human bladder carcinoma cell line, 5637, could act synergistically with interleukin-3 (IL-3) to increase the number of colonies formed in methylcellulose cultures by mouse hematopoietic progenitor cells. Subsequently this factor was identified as interlukin-1α (IL-1α). Thus, while its role in immunoregulation and inflammation has been well documented, only recently have we recognized that IL-1 is an important factor in hematopoiesis[1]. Recent evidence also indicates that IL-1 stimulates the growth of some tumors including acute myeloblastic leukemia cells.

To investigate the synergistic activity of IL-1α in more detail, we infected mouse bone-marrow cells with a retrovirus expressing the mouse IL-1α gene and subsequently "passaged" the cells in suspension cultures in the presence of IL-3. By four months, the cultures consisted of rapidly proliferating heterogeneous populations of cells; in contrast uninfected control cultures were comprised of homogeneous populations of slowly dividing mast cells. Preliminary analysis of the retrovirally-infected cells by histochemical techniques for enzymes characteristic of different hematopoietic subpopulations does not yet permit a definitive lineage assignment.

To study the effect of constitutive IL-1α expression on hematopoietic progenitor cells in vivo, we infected hematopoietic cells with the IL-1α-containing retroviral vector and transplanted these cells into irradiated syngeneic recipients. Several months after injection, successfully-grafted recipients have notably higher numbers of circulating leukocytes than normal controls. One mouse, in which we have documented expression of the introduced IL-1α gene, exhibited 8- to 10-fold higher than normal levels of circulating leukocytes and also had massive neutrophil infiltration in spleen and bone marrow. To date, these mice have developed no neoplastic myeloproliferative diseases. We believe that further investigation of the hematopoietic systems of these mice may provide additional insight into the role of IL-1α in hematopoiesis and leukemogenesis.

This project is supported by grants from the National Cancer Institute of Canada, and The Arthritic Society.

REFERENCE

1. Moore MAS: Role of interleukin-1 in hematopoiesis. *Immunol Res* 1989; **8**: 165.

---

[*] CS-110-1.

[**] Career Scientist, OCTRF Ottawa Regional Cancer Centre; and Assistant Professor of Medicine and Microbiology and Immunology, University of Ottawa.

EXPRESSION OF PLATELET-DERIVED GROWTH FACTOR GENE IN THE BACULOVIRUS*

D.M. LOGAN** and C-Y. KANG†, *Ottawa, Ontario*

Conventional gene expression systems have used prokaryotic cells such as *Eschericha coli (E. coli)* to produce recombinant gene products. These recombinant products lack post-translational modification including glycosylation and phosphorylation, which might be important for full biological activity. We can now produce large quantities of recombinant gene product properly modified post-translationally using baculovirus, an invertebrate virus. The recombinant product is synthesized and secreted when the baculovirus – *Autographa californica nucleopolyhedrosis* virus – carrying a foreign gene is introduced into pural ovarian cells of the moth *Spodoptera frugeperida*[1].

In this study we are inserting the platelet derived growth factor gene into the baculovirus system to produce properly post-translationally modified protein product and to determine its biologic activity profile. Before the gene is inserted, both the upstream and downstream DNA sequences require modification. Double-stranded cross-over "linkers" are inserted to remove redundant DNA sequences, which might interfere with the expression of the protein product. At present, the upstream sequence has been modified and we are undertaking further modifications of this sequence because Dr. Kang has demonstrated that such modifications will increase the secretion of recombinant product in the baculovirus system[2]. Once the upstream and downstream modifications have been completed the modified gene will be inserted into the baculovirus; then we will isolate and evaluate the secreted product for its biological activity.

REFERENCES

1. Kang C-Y: Baculovirus vectors for expression of foreign genes. *In:* Maramorosch K, Murphy F, Shatkin AJ, eds. Advances in Virus Research. New York: Academic Press, 1988; 177.
2. Personal communication.

---

* CLS-001.

** Clinician Scientist, OCTRF Ottawa Regional Cancer Centre, General Division; and Assistant Professor of Medicine, University of Ottawa.

† Chairman and Professor, Department of Microbiology and Immunology, University of Ottawa.

KAPOSI'S SARCOMA – AN IN VITRO STUDY*

D.M. LOGAN**, C.A. IZAGUIRRE†, L.B. HUEBSCH†† and C-Y. KANG‡
Ottawa, Ontario

Approximately 30% of those with the acquired immunodeficiency syndrome (AIDS), particularly male homosexuals, develop epidemic Kaposi's sarcoma (EKS)[1]. As a multicentric disease, EKS appears in the skin, lymph nodes and mucosal membranes lining the gastrointestinal (GI) tract and bronchial tree. Significant morbidity results when EKS lesions ulcerate, cause lymphedema or obstruct the GI tract or bronchial tree; current treatments, if effective, induce only temporary remissions[2].

Effective therapy for other tumors has been based on the clinical and biological characteristics of the tumor. It was difficult to determine the biological characteristics of EKS in vitro because long-term cell cultures could not be maintained.

During the past 18 to 24 months, we have established and maintained three EKS-derived cell cultures from skin biopsies of three different patients. These cultures have been characterized for morphology, potential cell of origin and growth characteristics. Of particular note, we have observed that EKS-derived cell proliferation depends on heparin and endothelial cell growth factor and is enhanced by the addition of virus-free supernatant from HIV-infected HUT78 cells (paracrine growth factor) or EKS-derived cells (autocrine growth factor).

During the next three years, our investigations will focus on characterizing the paracrine and autocrine growth factor and evaluating the effect of the regulating proteins of HIV replication on the development and proliferation of EKS cells. The long-term goal of these investigations is to define the biological characteristics of EKS and to design effective therapy to reduce EKS morbidity.

REFERENCES

1. Friedman-Kein AE, Laubenstein LJ, Rubinstein P, et al: Disseminated Kaposi's sarcoma in homosexual men. *Ann Intern Med* 1982; **96:** 693.
2. Odajnyk C, Muggia FM: Treatment of Kaposi's sarcoma: Overview and analysis by clinical setting. *J Clin Oncol* 1985; **3:** 1277.

---

[*] CLS-001-1.

[**] Clinician Scientist, OCTRF Ottawa Regional Cancer Centre, General Division; and Assistant Professor of Medicine, University of Ottawa.

[†] Chief, Division of Infectious Immunology, Federal Centre for AIDS, Health and Welfare Canada; and Adjunct Professor of Microbiology and Immunology, University of Ottawa.

[††] Hematologist, Ottawa General Hospital; and Assistant Professor of Medicine, University of Ottawa.

[‡] Chairman and Professor, Department of Microbiology and Immunology, University of Ottawa.

ADDITIONAL INVESTIGATIONS

Dr. W.K. Evans, Chief Executive Officer ORCC and Vice-President OCTRF, reports on the following clinical research investigations:

In 1988, 408 patients were entered on clinical trials at the Ottawa Regional Cancer Centre. Presently 66 active clinical protocols are accruing patients. The Centre is participating in NCIC, NSABP, pharmaceutical company and local studies. These studies include adjuvant chemotherapy of breast cancer, malignant melanoma, soft tissue and osteogenic sarcoma and colorectal carcinoma. Studies combining chemotherapy with radiation are underway in bladder carcinoma, glioblastomas, primary central nervous system lymphoma, head and neck carcinoma, cervix carcinoma, non-small-cell lung cancer, prostate and pancreatic carcinoma. Studies for chemotherapy in advanced or metastatic disease are underway in breast cancer, Hodgkin's disease, multiple myeloma, hairy-cell leukemia, gastric cancer, pancreatic cancer, renal-cell carcinoma, head and neck cancer, prostate carcinoma, glioblastomas, brain metastases, cervix carcinoma and non-small-cell and small-cell lung cancer. Also underway are a number of Phase I studies, pharmacology studies, and tumor biology studies. Studies are also being conducted of new antiemetics, anticipatory nausea and vomiting, factors important in patient decisions regarding trial participation, prophylactic antibiotics, analgesic bioavailability, megace in cachexia, Tantum cream for radiation skin reaction and for deafferentation pain, hyperthermia, new methods to reduce cisplatin renal toxicity and neurotoxicity, and nonchemotherapeutic agents as potentiators of chemotherapy. Radiotherapy studies are underway in breast cancer, prostate cancer, brain metastases, and non-small cell lung cancer.

MAGNETIC RESONANCE STUDIES OF GLIOMA CELLS AND TUMOR MODELS

Investigators: G.P. Raaphorst, D. Wilkins, J. McTavish, R.M. Kroeker, I. Smith and J. Saunders

p^{31} Spectroscopy. Results in the literature indicate that the stress caused by cancer therapeutic agents can cause changes in the high-energy phosphorous metabolites within cells. In this study we are investigating the p^{31} spectroscopy of rat glioma cells in vitro and in vivo. To date experimentation with the rat 9L cell line in vitro in a perfusion apparatus shows that these cells have a low level of PCR and high levels of ATP. A special probe is being constructed to evaluate the p^{31} metabolites in a brain tumor resulting from these cells implanted in the brain of Fisher-444 rats. Both cells in vitro and in the tumor are being evaluated for the responses to hyperthermia, radiation, chemotherapeutic agents and combinations of these.

Microimaging. A set of microimaging gradient coils, developed at the National Research Council of Canada, are being used to provide high resolution images of the rat 9L brain tumor. Image resolution is to voxel size – 40x40x150 micrometers. Detailed tumor morphology can be observed permitting us to evaluate the effects of treatment agents on early changes in brain and tumor morphology. These changes are being correlated with histological evaluation.

CLINICAL HYPERTHERMIA OF MALIGNANT DISEASE

Investigators: C.E. Danjoux, L.H. Gerig, G.P. Raaphorst, S. Grimes and A. Ginsburg

The literature indicates that hyperthermia can play a major role in the treatment of human cancer especially when combined with radiation or chemotherapy. At the Ottawa Centre, we are investigating a combination of microwave hypethermia and radiation. To date 20 patients have been treated in this manner. Radiation is applied using teletherapy or brachytherapy; hyperthermia is applied using an external 2450 MHz microwave applicator. The results are encouraging and point to the need to develop or acquire a hyperthermia system for deeper heating.

MEASUREMENT OF PORCINE-TISSUE BLOOD FLOW AND pH DURING HYPERTHERMIA

Investigators: L.H. Gerig, G.P. Raaphorst, C.E. Danjoux, G. Forester and P. Watson

Blood flow plays a major role in the removal of heat during the induction of clinical hyperthermia. In this project we are evaluating the response of blood flow in various porcine tissues as a function of heating time and temperature. Four methods of measurement are being employed: (1) blood flow measured in the arteries by a dye-dilution technique; (2) arterial blood flow measured by electromagnetic probe; (3) blood flow measured in tissues by radioactive microspheres lodged in capillary beds; and (4) measurement of temperature decay in microthermometry probes as a function of time. Initial results indicate that, in response to hyperthermia, the blood flow can vary as much as 20-fold and that temperatures above 44-45C will cause collapse in the blood flow response.

HYPERTHERMIA AND RADIATION: STUDIES ON INHIBITION OF CELLULAR REPAIR AND THERMORADIOSENSITIZATION IN HUMAN NORMAL AND TUMOR CELLS

Investigators: G.P. Raaphorst, M. Feeley, V.F. Da Silva, C.E. Danjoux and L.H. Gerig

Some cancers respond poorly to radiation and chemotherapeutic agents perhaps because these cells and tissues can repair the damage caused by such agents. This research project evaluates human-derived tumor cells such as glioma, melanoma and squamous cell carcinoma for their radiosensitivity in culture. We will attempt to correlate radiation response with ability to repair radiation damage. Hyperthermia is being used to induce radiosensitization and to inhibit repair of radiation damage. To date three glioma and two melanoma cell lines are being tested.

STUDY OF LONIDAMINE AS A RADIOSENSITIZER, THERMOSENSITIZER AND CHEMOSENSITIZER OF RODENT AND HUMAN CELLS IN CULTURE

Investigators: G.P. Raaphorst, C.E. Danjoux, J. Maroun, M. Feeley and L. Martin

Traditionally lonidamine has been used as a contraceptive agent, specifically a spermaticide. Recent evidence indicates that this agent also may have therapeutic effectiveness in cancer. Our studies will test the effect of lonidamine itself on rodent and human cells. Also, lonidamine is being combined with radiation to determine its radiation sensitization properties and to determine whether it can inhibit the repair or radiation damage. In addition, we are evaluting its properties as a thermal sensitizer and a sensitizer when combined with other chemotherapeutic agents. Already we have completed studies on lonidamine combined with radiation on various human and rodent cell lines and studies on lonidamine combined with cisplatinum show enhancement in squamous cell carcinoma.

THERMOCHEMOSENSITIZATION IN HUMAN RESISTANT TUMOR CELL LINES

Investigators: V. Da Silva, M. Feeley and G.P. Raaphorst

Hyperthermia has been shown to play a major role in chemosensitization. Our studies are evaluating the effect of hyperthermia on several chemotherapeutic agents tested in human, resistant tumor cell lines. At present, we have shown that the effectiveness of chemotherapeutic agents such as cisplatinum, BCNU, AZQ and SHM can be increased by the application of hyperthermia to human glioma cell lines. Additional studies are being done with a BCNU-resistant variant to determine whether hyperthermia can overcome such resistance. The results indicate that moderate thermosensitization can be achieved in cell lines resistant to BCNU. This strategy also may apply to resistance to other chemotherapeutic agents.

STUDY OF RADIOSENSITIVITY OF LYMPHOCYTE AND LYMPHOBLAST CELLS DERIVED FROM PATIENTS UNDERGOING CANCER THERAPY

C.E. Danjoux and Associates, G.P. Raaphorst, J. Cygler and M. Feeley

It has been asserted that in general radiation doses delivered to patients are limited by the response of a subpopulation which is more sensitive than the mean or by the response of another subpopulation which may be more resistant. In general, observation of normal tissue response in radiosensitive patients can set the upper limit for radiotherapy doses in all patients. To determine whether such heterogeneity exists in the human population, we are studying the radiation response of lymphocytes and lymphoblasts derived from patients at the Ottawa Centre. These studies are bing done in collaboration with N. Gentner and D. Morrison of Atomic Energy of Canada, who developed and perfected the technique for such tests. We hope these data will indicate whether a heterogeneity in radiation response exists and then determine in advance which patients are being treated to their optimum dose and which may be receiving more than optimum radiation.

HIGH DOSE RATE RADIATION IN HUMAN CELLS

Investigators: J. Cygler, M. Feeley, G.P. Raaphorst, N. Klassen and C.K. Ross

We are studying response of human glioma cells to high dose rates of radiation under oxic and anoxic conditions. A linear accelerator at the National Research Council of Canada is the source of high dose rate electron pulses. To date, we have determined the plating efficiency of the cells on glass, and survival curves of cells plated on glass and on plastic, irradiated with 60Co. Survival curves of the cells irradiated with electron beams from a linear accelerator were studied under oxic and hypoxic conditions, using pulses of duration 2.5 sec and 40. No difference was found as compared with 60Co experiments. The oxygen enhancement ratio in glioma cells was about 2.0 – a figure that is considered low. It is being investigated further.

MEASUREMENT OF MEGAVOLTAGE *BREMSSTRAHLUNG* SPECTRA FROM 5-40 MeV ELECTRONS ON THICK TARGETS

Investigators: B. Faddegon, D.O.W. Rogers, C.K. Ross and G.P. Raaphorst

Electron *bremsstrahlung* cross-sections are required for a variety of applications in radiotherapy physics. Few measurements are available and the calculations are only accurate to about ±10%. This project measured the thick target *bremsstrahlung* spectra of 5-40 MeV electrons from a linear accelerator, differentially in energy and angle for targets covering a wide range of atomic number. Measured spectra will be compared to Monte Carlo spectra to establish the accuracy of the calculation approach.

This measurement system has been used to obtain relative cross-section spectra of 10 and 30 MeV electrons on aluminum and lead targets at normal incidence (0° and 10°). Measured spectra shapes and relative cross-sections agree well with the Monte Carlo results. Improved energy calibration techniques have been explored and employed. Most recently we have achieved the capability of absolute cross-section measurement to better than a few per cent. A comprehensive set of cross-sections should soon be available.

COMPARISON OF ELECTRON DOSE DISTRIBUTIONS IN ANTHROPOMORPHIC PHANTOMS WITH CALCULATIONS DONE WITH THERAPLAN AND TARGET TREATMENT PLANNING SYSTEMS

Investigators: J. Cygler and J. Ross

Electron dose distributions in an anthropomorphic (Rando) phantom were measured using TLD-100 rods. CT scans of the head and chest wall sections of the phantom were done using a GE-8800 scanner.

We compared the measured doses for Therac-20 at a number of electron energies with isodose distributions calculated with Theraplan and Target treatment planning systems. Both programs perform inhomogeneity corrections based on pixel by pixel data but employ different physical models.

We compared the differences and similarities between performances of Theraplan and Target and these are discussed in terms of assumption inherent in both algorithms.

This study is carried out in collaboration with J.R. Cunningham and J. Jezioranski of the Ontario Cancer Institute in Toronto, and M. Evans of the Montreal General Hospital.

COMPUTER CONTROLLED RADIOTHERAPY

Investigators: D. Salhani, L. Gerig, G.P. Raaphorst, J. Cygler, M. Soubra and A. Girard

Improved effectiveness in radiotherapy can be achieved by precisely conforming the radiation beam to the tumor volume. Ideally we could achieve this by knowing the exact tumor volume and controlling the motions and output of a linear accelerator to optimally radiate such a volume. We are planning experiments on computer controlled radiotherapy using the new Siemens KD2 linear accelerator being installed at the General Division. This project is in its infant stage. We have described several features of this large project which we will undertake. These include developing an overall supervisory computer system and a system to optically monitor patient position. We will work on an automatic setup and verification collision avoidance algorithms, couch control and interfacing with treatment planning and imaging systems.

CHARACTERIZATION OF TISSUE SUBSTITUTE MATERIAL IN ELECTRON BEAMS

Investigators: J. Cygler, J. Ross, D.W.O. Rogers and M. Soubra

We irradiated substitute materials for muscle, lung, card bone and soft bone with electron beams of various energies. Dose distributions were measured with ionization chambers and films. Monte Carlo program was used to calculate electron stopping powers in these materials. Absolute dose was calculated based on measurements and stopping powers values.

MEASUREMENT OF THE EFFECTIVE MTF OF MEGAVOLTAGE IMAGING SYSTEMS

Investigator: J. Szanto

A new method was developed to determine the MTF from the measurement of the edge-spread function including the scatter contribution from the tissue equivalent phantom. Also taken into account are the scattering conditions by this method, which contribute to the deterioration of portal images. This is an easy way to compare the imaging properties of different screen-film combinations. Using ASYST software, we developed a mathematical procedure for determining the MTF from the edge-spread function.

Thunder Bay Regional Cancer Centre

CLINICAL INVESTIGATIONS

Dr. J.F. Kotalik, Chief Executive Officer TBRCC and Vice-President OCTRF, reports on the following clinical research investigations:

CLINICAL TRIALS

In the past two years, the Thunder Bay Regional Cancer Centre has acquired a sufficient, stable component of oncologists and thus became able to commit itself to an active clinical trials program. With a relatively small patient population distributed over many communities in the vast area of Northwestern Ontario, it is not feasible to attempt an autonomous clinical research program; however, paticipation in trials conducted by large co-operative groups has been successful.

Through 1989, we were involved in a variety of studies of the treatment of common malignancies in both adjuvant and advanced situations. Our primary clinical research affiliation is with the National Cancer Institute of Canada Clinical Trials Group and we take part in CO.03 and MA.4 examining adjuvant therapy in high-risk colon cancer and breast cancer and HD.4 investigating Hodgkin's disease. We have reactivated our connection with the North Central Cancer Treatment Group through the Duluth Clinic in Duluth, Minnesota. This permits us to participate in a large number of co-operative trials, especially in those examining therapy of advanced carcinoma of the breast, colorectal and renal carcinoma, high-grade gliomas and in several investigations of symptom-control measures particularly antiemetic trials.

With several Canadian centres, we have investigated the value of lonidamine in carcinoma of the lung and have joined the Northeastern Ontario Oncology Program in Sudbury in a trial of chemotherapy for small-cell carcinoma of the lung. In the future we intend to develop a clinical trials program conducted between the three Northern Ontario oncology programs.

At present, our Centre is accruing patients for 31 clinical trials for various diseases; in all, about 5% of our new patients are entered on clinical trials protocols.

MEDICAL PHYSICS

For part of the past year, this department was short of staff and struggled with a significant increase in workload. However, the staff continues in its interest and commitment to research.

We have undertaken a comprehensive program of experimental electron dosimetry using, as a starting point, electron-beam data available for therapy purposes. We have measured the various dosimetry parameters used to describe clinical electron beams and compared these data to those derived from various accelerators and reported in the literature, particularly those units which employ varying methods of beam transportation and generation of broad electron beams. Also we have examined various methods of dosimetric measurements and their consistency using detectors and phantoms commonly employed in clinical radiotherapy. These data not only have clinical usefulness but also provide material for the examination of various mathematical models used to describe electron-dose distribution and their correlation with experimental results.

The second project, done in collaboration with the Department of Electrical Engineering of Lakehead University, examines the effects of ionizing radiation on semiconductor circuit elements. This project will investigate the properties of these logic circuit elements (programmability, soft and hard failures, power consumption, etc.) as a function of ionizing dose. This will permit a theoretical description and accurate prediction of the behaviour of those electronic devices in the radiation environment. We need data of this type in order to manufacture equipment capable of reliable operation under extreme conditions.

These projects and other work in progress are made possible by our academic affiliation with the Department of Medical Physics of Lakehead University. Part of the funding for this activity has been provided by the OCTRF's Harold E. Johns Studentship Program and the SEED Program of Canada Manpower.

PSYCHOSOCIAL ONCOLOGY

In 1985, collaboration between our Centre and Lakehead University led to the creation of a Working Group for Psychosocial Oncology. Because of this work, we were given a special endowment to support an investigator in this area. In September 1988, under a joint appointment with Lakehead University, Scott M. Sellick, Ph.D., C.Psych., began to develop a research program, as well as supportive services for cancer patients. He worked with a number of graduate students in psychology and, in the first year, the group has completed three pilot projects.

We have studied psychosocial morbidity associated with anticipation of and experience during follow-up visits to the Centre, satisfaction and "burnout" of our staff, and measures to alleviate psychological distress during chemotherapy. At present, members of the group are preparing a survey of physicians' opinions regarding the potential contributions of psychosocial intervention in the enhancement of the quality of life and the impact such intervention might have on disease course.

Our research team with representation from Departments of Medical and Radiation Oncology of the Thunder Bay Regional Cancer Centre and Lakehead

University, Department of Psychology meets regularly to review the pilot studies and develop new programs. We have contacted several Centres with a view to developing multicentre collaboration for prospective trials in the psychosocial area and are searching for external funding from both provincial and national agencies.

CANCER CONTROL AND CLINICAL EPIDEMIOLOGY

The continuing recognition of new cases of advanced carcinoma of cervix in our Centre suggests that not all women in our catchment area derive benefit from screening of cervical cytology. To investigate this hypothesis, we developed a case-control study to assess cervical cytology screening in this area between 1975-1985 and to measure its impact on the natural history of this disease. This study has accrued 180 women with invasive cervical cancer and 196 individually matched controls.

We presented the findings of this study at the national workshop for screening of carcinoma of the cervix and these are summarized elsewhere in this report. The study was made possible by locally designated donations to our Centre and by co-operation from volunteers of the Canadian Cancer Society. It was designed and carried out in co-operation with the Foundation's Division of Epidemiology and Statistics.

Toronto-Bayview Regional Cancer Centre

ANALYSIS AND MANAGEMENT OF B CELL LYMPHOMAS*

N.L. BERINSTEIN**, *Toronto, Ontario*

My research program includes the following projects which compliment my clinical interests in non-Hodgkin's lymphomas.

Immunoglobulin Variation in B Cell Lymphomas

During the treatment of B cell lymphomas with monoclonal anti-idiotype antibodies it has been observed that an intrinsic feature of these lymphomas is variation of the immunoglobulin idiotype expressed on these cells. This project will study immunoglobulin variation on committed B cells at a molecular level in order to understand how the mechanisms of variation are controlled and how these mechanisms may differ with the level of differentiation of the B cell from which the lymphoma arose. We will use a well-characterized cell line, OCILY8, in which there is ongoing lambda gene rearrangements to study issues related to allelic exclusion and expression, and issues related to the control of lambda V gene utilization.

Assessment of Minimal Residual Disease in Non-Hodgkin's Lymphomas by Polymerase Chain Reaction Amplification of t(14:18)

This project will assess the ability of the polymerase chain reaction (PCR) – a recently described molecular technology – to detect lymphoma cells bearing the t(14:18) translocation that are not detectable by standard clinical techniques. We will develop a quantitative PCR assay to determine whether lymphoma cells can be detected by the PCR when there is no other clinical evidence of lymphoma. Complete response rate and time to progression will be correlated with the quantitative value of the PCR product found in blood and bone marrow at diagnosis and at time of complete response. Also we will compare results of the PCR product from blood versus bone marrow and the relative sensitivities of PCR amplification performed on genomic DNA to amplification of mRNA.

Biologic Prognostic Factors in Non-Hodgkin's Lymphomas

Advances in molecular immunology and molecular genetics have defined a number of biologic features of lymphoma cells and of the host's response to the lymphoma.

---

* CLS-003.

** Clinician Scientist, OCTRF Toronto-Bayview Regional Cancer Centre; and Assistant Professor of Medicine, Oncology, and Immunology, University of Toronto.

Dr. Carol Sawka and I have organized a collaborative effort to assess the prognostic importance of these biologic variables in all new lymphoma patients seen at the Toronto-Bayview Regional Cancer Centre Lymphoma Clinic. Some of the variables to be assessed will include assessment of the t(14:18) translocation in blood and bone marrow by Southern blot and by PCR, quantitative evaluation of expression of certain oncogenes and determination of the Ig V region used in the lymphoma's Ig rearrangement. This latter project will be done in association with Dr. K. Siminovitch (Assistant Professor, Department of Medicine and Immunology– University of Toronto).

Therapy of Relapsing B Cell Lymphoma with Monoclonal Pan B Cell Antibody and IL-2

It is known that, in murine models of B cell lymphoma, concomitant infusions of monoclonal antibody and IL-2 can produce dramatic and synergistic tumor lysis. Dr. Carol Sawka and I propose to test this approach clinically in patients with relapsing non-Hodgkin's lymphoma who have failed conventional chemotherapy. We will study the therapeutic effectiveness of these two agents with special attention to toxicity. Detailed immunologic monitoring will be done on all patients including assessment of serum levels of the infused antibody, alterations in the numbers and function of effector cell subsets in the peripheral blood, development of human antimouse antibodies and anti-IL-2 antibodies and assessment of B cell reconstitution after therapy.

An additional project will employ "homologous recombination" to engineer a mouse-human chimeric pan B cell antibody for eventual clinical testing.

ADDITIONAL INVESTIGATIONS

Dr. R.D.T. Jenkin, Chief Executive Officer T-BRCC and Vice-President OCTRF, reports on the following clinical research investigations:

ASSESSMENT OF MINIMAL RESIDUAL DISEASE BY POLYMERASE CHAIN AMPLIFICATION OF t(14:18)

Investigator: N. Berinstein

This clinical protocol is directed to the detection of otherwise non-clinically detectable minimal residual disease in blood or bone marrow of patients with low and intermediate grade lymphoma. A new and sensitive molecular technology, called the polymerase chain reaction, will be employed to amplify across the translocation breakpoint in malignant cells which have this translocation. The study will enroll patients attending the Toronto-Bayview Regional Cancer Centre/Lymphoma Clinic and blood and bone marrow samples will be obtained for analysis at diagnosis and at the time of complete response. The value of this quantitative assay will be correlated with the ability to obtain a complete response, with time to disease progression and with overall survival.

INTRAPERITONEAL (IP) ADMINISTRATION OF RADIOLABELLED ANTIBODIES

Investigators: R. Buckman, C. de Angelis, P. Shaw, R. Reed, H. Michaels, J. Law, R. Reilly, I. Kerr and A. Marks

These workers have investigated therapy of drug-resistant malignant ascites in recurrent ovarian carcinoma using monoclonal antibodies (MoAb) labelled with 131-I. From a panel of 21 MoAb, one (2G3, Cetus Laboratories) was selected for density and uniformity of staining of most cells in all effusions from patients with cancer of the ovary or breast. The cells were labelled with 131-I using N-bromo-succinamide which produced 95% incorporation of 131-I with 60-70% bioreactivity. Eleven patients received tracer doses of 2mCi injected IP for dosimetry, followed by therapeutic injections in Phase I design from 7mCi to 50mCi. Biopsy in two patients showed tumor/normal tissue ratios of 4.87 (mean) at 5 days and 1.64 at 13 days. Pharmacokinetic data showed mean biological half-life of radioconjugate IP was 252 hours (range 24-859 h). Average dose to bone marrow was 1.3 rad/mCi. Toxicity was minimal, comprising minor transient skin rash (two patients) and transient lowering of hemoglobin (95 g/l to 80 for two weeks, one patient). At the 50mCi dose level, two patients had temporary palliation of ascites.

RANDOMIZED STUDY OF TWO DOSES OF ABDOMINOPELVIC RADIOTHERAPY IN EARLY-STAGE EPITHELIAL OVARIAN CANCER

Investigators: A. Dembo, J. Sturgeon and R. Bush

This study, being conducted at the Toronto-Bayview Regional Cancer Centre and the Princess Margaret Hospital, seek the optimal dose for abdominopelvic radiotherapy in ovarian cancer, based on a dose-control vs dose-complication analysis. Accrual will be complete early in 1990.

PIGMENTED SKIN LESIONS AND MALIGNANT MELANOMA

Investigators: N. Iscoe, N. Lassam, L. From, M. McKenzie, J. Jambrosek, J. Gruss, J. Semple, T. Myhr, S. Hume and C. Levington

Through a computer-based malignant melanoma and dysplastic nevus registry, the investigators continue to monitor the clinical course of all patients with these conditions. Projects for the coming year include using the registry to identify control cases for patients developing recurrent disease, despite having had a shallow melanoma. The pathologic determinants will be reassessed in the cases and controls in a blind fashion. The registry data also will be used to compare different multivariate techniques in the identification of prognostic factors, namely, proportional hazards analysis versus recursive partitioning analysis. The pilot chemotherapy trial using VP-16 and platinum will be assessed and compared to similar studies being performed in Vancouver and New York.

BRACHYTHERAPY AND RADIATION PROTECTION PRACTICES AT THE TORONTO-BAYVIEW REGIONAL CANCER CENTRE

Written, narrated and produced by R.A. Siwek

This educational video is in two forms. All information is on a single tape and, in addition, is provided on three shorter tapes for more convenient viewing. The three shorter tapes are entitled: treatment types and techniques used in brachytherapy; radiation protection information; and dose equivalent limits and comparison of risks. The first section discusses in detail the principle of the Selectron – a remote afterloading device, manual afterloading with iridium-192 seeds and permanent implantation of iodine-125 seeds. The second section shows how one should handle sources and sets out guidelines for dose limitations. Finally, the third section states the dose equivalent limits for radiation, non-radiation workers and members of the general public. It compares the risk of receiving a given radiation dose to other risks that people face in their daily lives and have little or no control over.

A PHASE I-II PROTOCOL FOR HUMAN IMMUNODEFICIENCY VIRUS-ASSOCIATED NON-HODGKIN'S LYMPHOMA

Investigators: C.A. Sawka and F.A. Shepherd

These investigators have developed a Phase I-II protocol for the management of AIDS-related non-Hodgkin's lymphoma. This 12-week regimen uses weekly alternating sequences of myelosuppressive and nonmyelosuppressive drugs. Routinely, biweekly intrathecal injections are given to prevent lymphomatous meningitis and also aggressive antibiotic prophylaxis against Pneumocystitis carinii pneumonia and candidiasis. The endpoints include assessment of the toxicity and feasibility of the regimen, and evaluation of response rates and durations and of overall survival. The trial has been open to accrual since July 1, 1989. We expect to accrue 30 patients over a three-year period. The trial hopes to identify an active but well-tolerated regimen which then can be incorporated into a subsequent randomized controlled trial of treatment for AIDS-related non-Hodgkin's lymphoma.

DEVELOPMENT OF AN ND-YAG LASER SYSTEM FOR SPATIALLY CONTROLLED HYPERTHERMIA

Investigators: R.A. Siwek, D. Wyman, C. Swift and B. Wilson

These investigators are developing a practical approach to temperature control in tissue using multiple optical source fibres and a computer program which uses excitation – response data obtained from implanted microthermocouples to direct laser light down the implanted source fibres in an algorithmically determined order. Our multiple source and sensor approach coupled with the algorithmic incorporation of control theory achieves stable, optimal temperature control in a ground-beef phantom. Shortly we will test the method in a live animal model.

A RANDOMIZED PHASE III STUDY OF RADIATION AND 5-FU VERSUS RADIATION ALONE IN ADVANCED CARCINOMA OF THE CERVIX

Investigators: G.M. Thomas, A.J. Dembo in collaboration with the Princess Margaret Hospital, the London Regional Cancer Centre and the Ottawa Regional Cancer Centre

The survival of patients treated with radiation for carcinoma of the cervix has not seen substantial improvement since the 1950s. Improved pelvic control using radical conventional pelvic irradiation is hindered by the late complications in normal tissues.

Because 75% of patients who fail after conventional irradiation have uncontrolled pelvic disease, this study seeks to determine whether concurrent 5-FU chemotherapy and partially hyperfractionated irradiation will yield improved pelvic control rates, improved survival, and decreased complication rates in patients with advanced carcinoma of the cervix. The study is a four-arm trial in which standard radiation is compared to three study arms: Standard radiation with 5-FU; partially hyperfractionated radiation; and partially hyperfractionated irradiation plus 5-FU. The combination of partially hyperfractionated irradiation and 5-FU was submitted to an extensive "pilot" in Phase I, II studies over the past four years; in these 200 patients were studied to determine an acceptable regimen for concurrent chemotherapy and radiation.

This study, which accrued 109 patients to date, continues.

STUDY OF POSTORCHIECTOMY SURVEILLANCE IN STAGE I TESTICULAR SEMINOMA

Investigator: G.M. Thomas

When treated with adjuvant radiation following orchiectomy, cure rates for well-staged patients with Stage I seminoma are in the order of 99%. Surgical data and improvements in radiologic imaging of the retroperitoneum suggest that, when all staging tests are negative, less than 10 to 15% of patients actually have disease beyond the testicle. This means that 85 to 90% of these patients are receiving unnecessary radiation.

Therefore it is appropriate to study the effect of surveillance only in patients with Stage I seminoma because we expect salvage of relapsing patients to produce cure rates equal to those achieved by treating all patients initially with radiation.

This study, which continues, seeks to determine the cure rates and relapse rates in patients on surveillance and determine whether placental alkaline phosphotase is useful marker for following patients with testicular seminoma. The initial specimen will be subjected to careful pathologic review to identify any pathologic prognostic factors, which may predict relapse after orchiectomy.

A PHASE III STUDY TO DETERMINE WHETHER THE ADDITION OF STRONTIUM-89 THERAPY TO STANDARD FRACTIONATED LOCAL FIELD IRRADIATION IS MORE EFFICACIOUS THAN LOCAL FIELD IRRADIATION IN THE MANAGEMENT OF ENDOCRINE-RESISTANT METASTATIC PROSTATE CANCER: A TRANSCANADAMULTICENTRE STUDY AT TORONTO-BAYVIEW REGIONAL CANCER CENTRE

Investigators: G.M. Thomas, A.T. Porter and A.J. McEwan

Palliative radiation for painful bony metastases is standard therapy for metastatic prostate cancer that has resisted endocrine manipulation. In general, these patients have multiple osseaous metastases and usually require wide-field radiation or multiple separate treatments for different sites of disease. This study seeks to determine whether intravenous Strontium-89 successfully palliates painful prostate osseous metastases and leads to improved quality of life and decreased need for external radiation. Strontium-89 is a calcium imitator that is not incorporated into marrow or leukocyte. It is selectively taken up in areas of bone, which is the site of increased turnover; this includes sites of bony metastases.

Patients with multiple bony metastases receive palliative external irradiation to one or two sites of known disease and then are randomized to receive either a tracer dose of Strontium-89 (placebo) or a therapeutic dose. Patients will be followed to determine whether there is any slowing in the progression of asymptomatic metastases, to evaluate the analgesic efficacy of intravenous Strontium-89 and to document the morbidity of Strontium-89. Survival of patients treated with Strontium-89 will be compared to those receiving the tracer dose (placebo).

DOSIMETRY OF RADIOLABELLED MONOCLONAL ANTIBODIES FOR TREATMENT OF MALIGNANCY

Investigators: M.K. Woo, P. O'Brien and R. Reed

Radioimmunotherapy, a relatively new mode, treats malignancies by injecting into patients antibodies with attached radionuclides. These "monoclonal" antibodies may have a high specificity to target tumor sites; if so, the radionuclides will deliver radiation to destroy tumor cells. The amount of radiation, however, has to be controlled carefully to minimize damage to normal tissues. Curent methods of dose calculation are based on computer modelling and little measurement data are available. This project is part of our ongoing plan to develop a reliable system for radiolabelled monoclonal antibody dosimetry. For this project, we submerge radiation-sensitive material —thermoluminescent dosimetry (TLD) chips in a solution containing radioactive substance; then we examine the radiation received by the TLD chips as a function of various parameters, such as the type of radionuclide, size of TLD chips, exposure time, etc. The results may serve as a benchmark for existing and new physical and mathematical models of radioimmunotherapy dosimetry.

STEREOTACTIC RADIOSURGERY

C. Young, M. Schwartz, P. Davey, P. O'Brien and B. Gillies

The stereotactic radiosurgery facility at the Sunnybrook Medical Centre/Toronto-Bayview Regional Cancer Centre is based upon a design described by I. Podgorsak in Montreal. The treatment involves simultaneous rotation of a linear accelerator couch and gantry around a target that is located at the isocenter of rotation. We determine target coordinates and generate dose contributions using software developed at the Montreal Neurological Institute.

The Sunnybrook Medical Centre system has several unique features. We have made extensive modifications to the linear accelerator drive systems to allow automatic couch and gantry rotational synchrony regardless of gantry speed. The absorbed dose rate at the target is increased by a factor of 2.8 by removing the beam flattening filter so that the treatment time is now less than eight minutes. We do routine pretreatment verification of isocentric integrity and have developed a stand-alone electronic interlock system to monitor machine settings.

To date nine patients have been treated with our system. Usually, the entire procedure including frame attachment, localizing angiograms, CT scans, treatment planning and dose delivery normally can be completed in less than one day.

PHARMACOKINETICS OF FOLINIC ACID AND 5-FLUOROURACIL IN PATIENTS WITH COLORECTAL ADENOCARCINOMA ON TREATMENT WITH THIS COMBINATION

Investigators: G. Bjarnason, C. Erlichman, I. Kerr, J. Thiessen and P. Bunting

The combination of 5-fluorouracil (5-FU) and folinic acid (FA) is active in the treatment of metastatic colorectal cancer. At Phase II trials, this combination shows improved response rate and survival when compared to 5-FU alone. Adjuvant trials are ongoing. In spite of a flurry of clinical activity, few workers have done pharmacological studies of FA. Commercially available FA preparations consist of a racemic mixture of l-FA and d-FA. Only the l-form is biologically active and there is evidence that the d-form may interfere with the activity of the l-form. In our pharmacokinetic study of 5-FU and d,l-FA, patients on this 5-day treatment have blood drawn for pharmacokinetics on days 1 and 4 over an 8-hour period. Our objectives are to define the disposition of FA and 5-FU on days 1 and 4 and to correlate these data with evidence of hematological and gastrointestinal toxicity.

We are participating in an international Phase II trial of 5-FU and l-FA. Patients on this study get one-half the dose of the biologically active l-form (compared to those getting the d,l-form) but the same dose of 5-FU. In conjunction with this Phase II trial, we will do another pharmacokinetics study of 5-FU and l-FA using the same design as in our previous study. This will allow us to compare pharmacokinetic and pharmacodynamic data in this study with that from our previous study of the d,l-form, thus it will help us decide whether clinically the l-form is superior to the d,l-form. These studies are being done jointly at the Toronto-Bayview Regional Cancer Centre and the Princess Margaret Hospital.

In conjunction with these studies, G. Bjarnason will develop in C. Erlichman's laboratory an HPLC assay for FA, its metabolites and its isomers.

A PROSPECTIVE RANDOMIZED STUDY OF TAMOXIFEN COMPARED TO TAMOXIFEN PLUS SIX MONTHS OF CMF IN POSTMENOPAUSAL WOMEN WITH AXILLARY NODE-POSITIVE BREAST CANCER

Investigators: K.I. Pritchard, S. Fine and A.H.G. Paterson

A co-operative group from Toronto and Edmonton, including the present authors and several other investigators, undertook a prospective randomized study of breast cancer in postmenopausal, axillary-lymph-node-positive women; they received either tamoxifen 30 mg daily for two years or tamoxifen 30 mg daily for two years plus cyclophosphamide, methotrexate and 5-fluorouracil (CMF) every three weeks for eight treatments – about six months. The original sample size was 300 patients. Initial funding was obtained from the Medical Research Council of Canada. Within a few months of the trial's opening in 1984, the Clinical Trials Group of the National Cancer Institute of Canada (NCIC) joined the core investigators for a multicentre, crossCanada study with data co-ordination by the Clinical Trials Group Office. Dr. Pritchard is study chairman, Drs. Paterson and Fine are members and the other work through the NCIC Clinical Trials Group Protocol Committee. The Medical Research Council of Canada continues to provide core funding.

Because this group of patients has an extremely favorable survival, the group decided to increase the sample size to 700 patients to improve the power of the study. Over 600 patients have been randomized but no formal analysis will be done until accrual has been completed. The NCIC Clinical Trials Group, under the guidance of Drs. Pater and Pritchard, will provide quality control and toxicity monitoring.

THE ROLE OF NEU ONCOGENE AMPLIFICATION AND FLOW CYTOMETRIC MEASUREMENTS AS PROGNOSTIC VARIABLES IN PREDICTING RELAPSE AND SURVIVAL IN WOMEN WITH AXILLARY-NODE-NEGATIVE BREAST CANCER

Investigators: K.I. Pritchard, M.E. Trudeau, I.L. Andrulis, W.H. Hanna, H.L. Lickley, G.B. Mobbs, D. Murray and C.A. Sawka

The most important predictor for relapse in breast cancer is the presence of metastatic disease in axillary lymph nodes at the time of initial surgery. Although women with axillary-node-negative disease have a lower risk of relapse than their node-positive counterparts, a proportion of node-negative women will relapse and ultimately will die of breast cancer. We desire to identify this subgroup of node-negative women at high risk of relapse because they should be targeted for trials of adjuvant therapy.

We are analyzing the prognostic importance of neu oncogene amplification and measures of cancer-cell activity (flow cytometric measurement of % S phase and DNA content) in 432 women with node-negative breast cancer. These women are a subset of the Henrietta Banting Breast Centre database, which consists of all women with primary breast-cancer surgery done at Women's College Hospital in Toronto from 1977-1986 inclusive. In addition to these experimental factors, we will examine by multivariate analysis other factors believed to be prognostic for relapse and death. The Ontario Ministry of Health has allocated $126,938 for this study which began in April 1989. We are proceeding with the molecular assays and the database contents are being "cleaned up" and made ready for analysis.

Division of Epidemiology and Statistics, Toronto

EPIDEMIOLOGY RESEARCH UNIT[*]

E.A. CLARKE[**], E. HOLOWATY[†], N. KREIGER[††], L.D. MARRETT[‡]
and J. McLAUGHLIN[‡‡]
Toronto, Ontario

Since 1978, the Epidemiology Research Unit of the Division of Epidemiology and Statistics has been affiliated with the Department of Preventive Medicine and Biostatistics at the University of Toronto. The Unit was established to conduct analyses using the cancer-data bases of the OCTRF, to assess the quality of these data, to provide cancer research workers with epidemiological and biostatistical assistance, to conduct or support cancer research projects, and to provide information on cancer to the general public and the scientific community.

Members of the unit, holding academic appointments at the University, are Drs. E.A. Clarke, E. Holowaty, N. Kreiger, L.D. Marrett and J. McLaughlin. Other staff members are G. Cameron, I. Fan, J. Fleury, S. Hilditch, D. Nishri, K. Rentner, T. Sardinha and M. Swift. Additonal Unit members who are supported by externally funded research projects are: D. Bijelic, S. Chin Cheong, K. Easun and S. Ferrier

The Unit provides the site for many of the externally-funded research projects of the Division of Epidemiology and Statistics. Recently, etiologic case-control studies of malignant melanoma, renal-cell carcinoma, thyroid cancer, bone cancer, malignant germcell cancer, and lymphoma and soft-tissue sarcoma have been conducted here. Many of these studies used the Ontario Cancer Registry to identify cases and involved collaboration with other investigators and agencies.

Staff of the Unit have participated in many projects based on the Ontario Cancer Registry, such as: Survival analyses for various types of cancer; preparation of a cancer mortality atlas for Ontario; investigation of the risk of congenital anomalies in the offspring of cancer patients; review of the quality of data in the Registry; and investigation into identifying native people in the Registry to permit the study of their cancer patterns.

---

[*] Project 381.

[**] Head, Division of Epidemiology and Statistics, Ontario Cancer Treatment and Research Foundation; and Associate Professor in the Department of Preventive Medicine and Biostatistics, University of Toronto.

[†] Head, Cancer Registration Unit, Division of Epidemiology and Statistics, OCTRF; and Assistant Professor in the Department of Preventive Medicine and Biostatistics, U of T.

[††] Head, Statistics Section, Division of Epidemiology and Statistics, OCTRF; and Assistant Professor in the Department of Preventive Medicine and Biostatistics, U of T.

[‡] Director, OCTRF Epidemiology Research Unit; and Assistant Professor in the Department of Preventive Medicine and Biostatistics, U of T.

[‡‡] Senior Epidemiologist, Division of Epidemiology and Statistics, OCTRF; and Lecturer in the Department of Preventive Medicine and Biostatistics, U of T.

In addition, analyses are being carried out using data collected during case-control studies conducted by senior Epidemiology Research Unit staff in past years. These include examination of the association between cigarette smoking and endometrial neoplasia; the risk of malignant melanoma associated with constitutional factors; and the effect of follow-up procedures on estimates of relative risk in case-control studies based on postal questionnaires.

There has been extensive development of microcomputer software to display the data being generated by the Ontario Cancer Registry. These include graphs of time trends in the incidence or mortality of various types of cancer, maps of cancer mortality by county, and calculation of rates for specified subgroups of patients. These have been useful in investigating the patterns of cancer in Ontario.

Staff of the Research Unit organized the OCTRF's 1989 Cancer Epidemiology Seminar. This year's themes were: "Primary Prevention of Cancer" with Dr. G.B. Hill of McGill Univerity, Dr. J. Birdsell of the Alberta Cancer Board, and Dr. K.S. Brown of the University of Waterloo; and "Cancer Etiology" with Dr. W.E. Rawls of McMaster University and Dr. L. Ritter of Health and Welfare Canada. This one-day seminar drew over 100 attendees from government departments and agencies, universities, and health care institutions.

Finally, those with academic appointments have been involved in teaching of undergraduate medical students and graduate students (M.Sc. and Ph.D. candidates) in epidemiology.

This project is supported by the OCTRF.

ADDITIONAL INVESTIGATIONS

Dr. E.A. Clarke, Head, Division of Epidemiology and Statistics, and Vice-President OCTRF reports on the following studies:

CHILDHOOD LEUKEMIA AROUND NUCLEAR FACILITIES

Investigators: E.A. Clarke, T.W. Anderson and J.R. McLaughlin
This study will determine whether clusters of childhood leukemia exist in children born to mothers residing in the vicinity of major nuclear facilities in Canada, the majority of which are in Ontario. It was initiated in response to findings in the U.K. of childhood leukemia clusters near two nuclear installations.

In the initial phase of the study, all children, aged 0-4 years, who died from or developed leukemia were identified from both the mortality file (1950-1986) and the incidence file (1964-1985) of the Ontario Cancer Registry. The birth certificates of these children were used to determine the mother's residence at the time of the child's birth. The annual number of live births, by mothers' residence in the five counties of interest, were obtained from Ontario Vital Statistics. The rate of leukemia in relation to live births was calculated for each area and compared with the provincial rate. The preliminary analysis indicated that slightly more leukemia occurred than was expected; however, even with the long period covered by this study, there were few cases and the excess could have been due to chance alone. To improve the precision of the results, the study has been expanded to examine the occurrence of leukemia in children up to age 14. Analyses of these data are underway.

The project is funded by the Atomic Energy Control Board.

CARDIAC CATHETERIZATION AND THE RISK OF CANCER: A FOLLOW-UP STUDY

Investigators: N. Kreiger, J. McLaughlin, S. Hilditch and E.A. Clarke
Children with congenital heart disease, who undergo cardiac catheterization, may receive significant radiation exposure during multiple chest fluoroscopies. Compared to the general population, this study evaluates the risk of cancer in later life among those with childhood exposure to cardiac catheterization.

Patients, who were catheterized at the Hospital for Sick Children (HSC) in Toronto between 1950 and 1965, were linked with the Ontario Cancer Registry incidence file (1964-1985) and with the Ontario death file (1950-1985). Rates of cancer in these patients will be compared with those of the general population. If an excess of cancer is identified in the catheterized group, a "nested" case-control study may be conducted to assess in more detail the factors associated with risk.

Study subjects have been identified from computerized data files at HSC. These have been linked with Ontario marriage license files to identify alternative surnames. Linkage with cancer incidence and death records also is complete. Data are being analyzed to assess the relative frequency of cancers in the cohort, compared to that expected for the population at large.

This project is funded by the Atomic Energy Control Board.

A POPULATION-BASED COHORT STUDY OF THE PROGNOSTIC IMPORTANCE OF STEROID RECEPTORS IN BREAST CANCER

Investigators: E. Holowaty, J. McLaughlin and T. Piscione

We conducted a population-based cohort study in Ontario to assess the prognostic importance of estrogen (ES) and progesterone (PR) receptors in predicting overall survival in breast cancer. The Ontario Cancer Registry was used to identify 3136 breast cancers, newly diagnosed in 1981, in Ontario women under 80 years of age who were eligible for the study. The diagnosis was verified histologically for 93.2% of the subjects: ER and PR assays were available for 71.5% of the cohort.

From histopathology reports, we classified each case according to nodal status, i.e., 0, 1-3 or >3 nodes and tumor size <2 cm, 2-5 cm or >5 cm. Overall survival was determined to December 31, 1986, at which time 36.6% of the eligible subjects had died due to any cause. We examined the prognostic significance of ER/PR using survival analysis, while controlling for the effects of other known prognostic factors, e.g., nodal status, tumor size, menopausal status.

Univariable analyses showed that each of ER, PR, nodal status, tumor size and menopausal status (age <50 or age ≥50) were significantly associated with survival. The five-year survival rate was 77% for women who were ER positive and 64% for women who were ER negative ($p<0.001$). The results were similar for PR. The ER and PR classes continued to have prognostic significance while controlling for nodal status, tumor size and menopausal status. We found only a small differential in survival between ER/PR classes in patients with early stage disease, e.g., with no nodal involvement, whereas there was a large and significant differential among women with the most extensive disease, e.g., among 300 patients with >3 nodes involved, five-year survival for ER+ = 60% and for ER- = 27%; $p<0.001$. Detailed multivariable analyses are underway. These results demonstrate that ER and PR levels can predict survival, particularly in patients with more extensive disease.

RADIATION EXPOSURE AND BONE CANCER

Investigators: N. Kreiger, M. Finkelstein, P. Beck and A. Lye

This population-based case-control study will provide information on the risk of bone cancer associated with radium content in drinking water. It also will address the risks associated with other factors, including prenatal and early childhood exposures. The study has two parts: one will concentrate on investigating the association between bone cancer and radium in drinking water; the other will examine the effects of several other potential risk factors. Cases comprise patients 25 years of age or younger with bone cancer in the Province of

Ontario. They will be identified through reports submitted to the Ontario Cancer Registry (OCR) between the years 1964 and 1988. There will be two control groups: one identified through OCR records, the other selected through random digit dialing of the telephone. Controls will be of the same age and sex as the cases.

Mothers of subjects given this diagnosis before 1980 will be asked to complete a brief questionnaire concerning their residence history; mother of subjects diagnosed since 1980 will complete a more detailed questionnaire regarding the subjects' prenatal and childhood exposures. With the knowledge of the subjects' mothers, water samples will be taken at their previous residences. Statistical analysis will be done to ascertain differences between cases and controls.

We have completed questionnaire development and have developed a microcomputer data management system. Cancer subjects (cases and controls) are being identified and located. Also population controls are being identifed, questionnaires are being sent out and follow-up initiated.

This project is funded by the Ontario Ministry of Health.

STEROID-RECEPTOR CONTENT AND THE EPIDEMIOLOGY OF BREAST CANCER

Investigators: N. Kreiger, W. King and E.A. Clarke

Evidence that the prognosis of breast cancer patients is associated with tumor estrogen and progesterone receptor levels has provoked interest in the epidemiology of breast cancer in relation to steroid receptors. This population-based case-control study looks at known and suspected risk factors for breast cancer according to tumor estrogen and progesterone receptor levels. The project is part of a multicentre collaborative study of primary breast cancer.

Eligible cases were women aged 20 to 69, who, between January 1982 and January 1986, had a histologically confirmed primary carcinoma of the breast and were referred to a cancer treatment centre in Metropolitan Toronto. These records were linked to the steroid-receptor files at the Ontario Cancer Treatment and Research Foundation to obtain steroid receptor data. Of 607 interviewed cases, 532 (88%) had had an eligible assay. We have collected interview data on 1214 controls matched 2:1 to cases by age and neighborhood of residence.

Within-case analysis is proceeding on demographic data, medical history, reproductive history, smoking and alcohol to detect associations between known risk factors and the tumors' steroid-receptor concentration. Matched case-control analysis is being carried out to quantify risks for breast cancer with high or low steroid-receptor content.

This project is funded, in part, by the Ontario Ministry of Health.

THE ETIOLOGY OF RENAL-CELL CARCINOMA IN ONTARIO

Investigators: L.D. Marrett, N. Kreiger, L. Dodds and S. Hilditch

In 1986, we began a case-control study of the etiology of renal cell carcinoma in Ontario. Patients with newly diagnosed cancer for the period 1986 and 1987 were sent a brief questionnaire requesting information on smoking, dietary habits, occupational exposures, use of analgesic and diuretic medications, and basic demographics. We sent the same questionnaire to a random sample of the population selected from enumeration records held by the Ontario Ministry of Revenue. Nearly 90% of cases and 74% of population controls responded – a very high rate of response for this type of survey.

Data collection is completed (513 cases and 1369 controls), and analysis has begun. As anticipated, cigarette smoking, obesity and use of diuretic medications increase the risk of renal-cell carcinoma. We hope that ultimately risk-factor modification will reduce the incidence of renal-cell carcinoma.

This project is funded by the Ontario Ministry of Health.

THE ETIOLOGY OF MALIGNANT GERM-CELL TUMORS

Investigators: L.D. Marrett and H. Weir

Usually malignant germ-cell tumors (MGCT) develop in the testis but also can appear in the ovary and at extragonadal sites, although less frequently. Most testicular cancers (TC) in males and ovarian tumors in females under age 15 are of germ-cell origin. In recent years, incidence rates have been rising for TC in Ontario and elsewhere. Also the childhood incidence of ovarian cancer and MGCT (of all sites) appears to be increasing for reasons that as yet are unknown.

This study is investigating the etiology of MGCT in Ontario. Cases, which are being identified through the Ontario Cancer Registry, constitute all Ontario residents diagnosed with MGCT between 1986 and 1989, age 59 or less. Age and sex stratum-matched controls have been selected from the assessment rolls of the Ministry of Revenue. Relevant exposure information is being collected through questionnaires sent to subjects and/or their mothers.

Some have suggested that the totipotentiality of germ cells in TC changes with age. This fact may have implications for the study of MGCT of all sites: for example, disease state according to histologic groupings, which correspond to the changing totipotentiality of the germ cells, may elucidate etiologic risk factors specific to these histologic subgroups. This study includes a slide review to achieve a uniform classification of all tumors. In addition, we will describe the detailed age, sex, site and histology distribution of these tumors in the population.

A collaborative analysis is also proposed with centres in Denmark and British Columbia/Alberta where similar studies on TC have been done recently or are being done. Descriptive analysis correlating exposure variables in the population with incidence of disease, where disease rates vary substantially, may provide insight into the international variability of TC incidence rate.

We expect to collect data on about 700 cases, 1300 controls and 1200 mothers. Response rates during the first year of the study have been gratifyingly high.

This project is funded by the Ontario Ministry of Health.

CONGENITAL ANOMALIES IN THE OFFSPRING OF CANCER SURVIVORS

Investigators: L.D. Marrett and G.J. Sherman

In many cancers of childhood and young adulthood, long-term survival and cure are now possible largely as a result of chemotherapy and radiation. While some late complications of cancer therapy have been recognized, little is known about the wellbeing of the offspring of cancer survivors.

We are conducting a case-control study to determine whether the offspring of former cancer patients are at an increased risk of congenital anomalies and, specifically, whether preconception cancer treatment (radiation and chemotherapy) is responsible for such an increase. Cases are defined as the parents of Ontario liveborn children recorded in the Canadian Congenital Anomalies Surveillance System (CCASS) between 1979 and 1986 and are identified from the birth certificates of their anomalous children. Controls are parents of a random sample of children not registered in CCASS, selected from Ontario livebirth certificates.

A computer linkage will be done between the case and control parents and the Ontario Cancer Registry to identify any cancer diagnoses made before the index birth and between 1964 and 1986. For all such cancers, we will seek information on cancer treatment (chemotherapy and radiation, and/or surgery) from the regional cancer centres, hospitals and physicians.

Relative risks associated with a history of cancer and type of therapy will be estimated. The results of this study may contribute information concerning potential adverse effects of cancer therapy in long-term cancer survivors.

This project is funded by the Ontario Ministry of Health.

GEOGRAPHIC VARIATION IN ONTARIO CANCER RATES

Investigators: S.D. Walter, L.D. Marrett, S.M. Taylor, J.D. Drake, J.A. Davies and M.V. Hayes

This study examines the spatial variation in incidence rates for the major cancer sites in Ontario, using sophisticated statistical techniques. County level cancer in incidence data from the Ontario Cancer Registry (OCR) for two time periods, namely 1964-1975 and 1976-1986, provide the basis for this study. Persistence of spatial patterns between the two time periods is being investigated.

As part of this project, we are evaluating the quality of residence information the OCR. In addition, for each county, we are estimating the number of cases which have not been ascertained by the OCR or which have no residence information; also we will examine the geographic patterns of "missingness".

An additional objective of the study is to investigate the feasibility of conducting a formal ecologic analysis relating cancer rates to environmental variables such as water quality, air contamination, degree of urbanization and industrialization.

Spatial and quality of data analyses have been completed for several major cancer sites, and we are studying the results. We have completed investigation into the existence, quality, and availability of environmental databases for ecologic studies.

This project is funded by the Ontario Ministry of Health.

LEUKEMIA AFTER RADIATION FOR UTERINE CORPUS CANCER

Investigators: E.J. Holowaty and P. Toogood

This population-based case-control study will provide information on the risk of leukemia among women treated with radiation for uterine corpus cancer (UCC). This study is being conducted by the Radiation Epidemiology Branch of the National Cancer Institute (NCI) in collaboration with population-based, cancer registries in Ontario, Los Angeles, Iowa, Michigan, Connecticut, Denmark, Finland and Norway.

Women diagnosed with uterine corpus cancer during the period 1964 to 1985 and who survived a minimum of 12 months were eligible for this study. Cases were selected from the subjects who had been diagnosed with leukemia at least 12 months after the diagnosis of uterine corpus cancer. Controls, subjects with UCC who did not have a second primary, were matched to each case (4:1) based on date of diagnosis of UCC, age and duration of leukemia-free survival. All study subjects were identified through the Ontario Cancer Registry.

Relevant study information, including the subject's medical history, treatment, vital status and reproductive history, was abstracted from hospital and clinic records. The data collection phase of this study began in January 1988 and was completed in March 1989.

Across all participating registries, data were collected for 203 cases and 737 controls. Ontario contributed 35 cases and 120 controls to this study. Dr. M. Stovall at M.D. Anderson in Houston, Texas, is reviewing the radiation dosimetry. Preliminary analysis of the entire study file has begun at the NCI. Overall, 65% of these subjects received radiation for UCC (61% of Ontario subjects). Of all subjects who received radiation, 54% received brachytherapy only, 22% received external-beam therapy only and 24% received both. For Ontario subjects, 79% received brachytherapy only, 2% received external-beam therapy only and 18% received both. As yet, there is no information about the relationship between radiation dose and risk of leukemia.

We hope to begin analysis of the Ontario portion of this study in the summer of 1990.

This project is funded by the National Cancer Institute, Bethesda, Maryland.

SECOND CANCERS FOLLOWING TREATMENT FOR UTERINE CORPUS CANCER

Investigators: E.J. Holowaty and P. Toogood

This population-based cohort study evaluates the risk of all second cancers following treatment for uterine corpus cancer (UCC). This study is being conducted by the Radiation Epidemiology Branch of the National Cancer Institute in collaboration with population-based cancer registries in Ontario, Denmark, Finland, Sweden and the U.S.A. (SEER). Observed and expected numbers of second primary cancers will be evaluated by time since diagnosis of UCC, age at initial diagnosis, histologic type of uterine cancer and type of treatment. In Ontario, all women are eligible who have been diagnosed with UCC between 1964 and 1987 and have not had a prior malignancy. Approximately 18,000 eligible subjects have been identified through the Ontario Cancer Registry. Information about date of diagnosis, age, tumor morphology and second primaries is readily available through the Ontario Cancer Registry, although some of this information will require confirmation. For the Ontario part of the study, we will be unable to collect treatment information. It is anticipated that approximately 1200 Ontario subjects will be confirmed to have a second primary. Data collection for this study began in October 1989 and will be completed by September 1990.

This project is funded by the National Cancer Institue, Bethesda, Maryland.

THE EFFECTIVENESS OF CERVICAL CYTOLOGY SCREENING IN NORTHWESTERN ONTARIO

Investigators: E.J. Holowaty, J.F. Kotalik, V. Hunter, V. Nguyen and J. Large

Recently, a population-based case-control study of women with invasive cervical cancer was conducted in Northwestern Ontario. The primary purpose was to assess the effectiveness of the cervical cytology (i.e. Pap smear) screening program. The study includes 118 women with invasive cervical cancer diagnosed between 1975 and 1985, who reside in Northwestern Ontario, and were 20-69 years of age at the time of diagnosis. These patients were matched with 196 controls, consisting of incident cases of all other cancers diagnosed in women residing in the same area over the same period; they were matched individually to cases, on the basis of age and date of diagnosis. Controls were excluded if they had a history of hysterectomy before the date of diagnosis. Both cases and controls were identified through the Ontario Cancer Registry and verified through chart review. Sociodemographic, diagnostic and Pap smear information was collected through review of patient charts in local public hospitals and in the Thunder Bay Regional Cancer Centre, through questionnaires mailed to attending physicians and through review of all cervical cytology log books maintained by the six laboratories serving Northwestern Ontario. Data collection was completed by December 1988 and analysis is now complete.

Approximately 63% of cases and 37% of controls never had a normal screening Pap smear. The risk of developing cervical cancer for "never-screened" women was threefold higher than "ever-screened" women. Approximately 40% of invasive cervical cancer over the period 1975-1985 could be attributed to the failure of women to have even a single Pap smear. The variables, sojourn time (i.e., time to last normal screening smear) and number of normal screening smears, both exhibited a strong dose-response relationship with the risk of cervical cancer.

No evidence was found of an appreciable improvement in the effectiveness of Pap screening over time, comparing the earlier period (1975-1979) with the later period (1980-1985). The odds ratio comparing "never" versus "ever", rose from 2.6 in the earlier period to 3.3 in the later period, perhaps because of better test performance. An appreciable proportion of smears taken in cases within two years of diagnosis were reported as normal (30%). This false negative rate was higher in the earlier period (41%) than in the later period (20%), suggesting an improvement in the quality of taking and/or reading the smears.

This study demonstrates that a substantial proportion of the recent burden of invasive cervical cancer in Northwestern Ontario is attributable to inadequate performance of the cervical cancer screening program. There is no good evidence that this performance is improving over time, although there is some evidence of improvement in the quality of taking and/or reading the smears. It is apparent that the recruitment into the program of women, who have never been screened, would lead to an appreciable reduction in risk.

University of Toronto

FACTORS AFFECTING URINARY MUTAGENIC LEVELS OF WORKERS WITH BLADDER CANCER[*]

B.C.K. CHOI[**] and J.G. CONNOLLY[†], *Toronto, Ontario*

The authors are carrying out a study to determine the usefulness of urinary mutagenicity screening in the identification of bladder cancer in workers in high-risk industries. They seek to determine whether it is reasonable to perform urinary mutagenicity testing in workers exposed to mutagenic substances. They also wish to determine if such testing is useful in the evaluation of individuals who have bladder cancer and in whom the disease may be due to workplace exposure.

The study involves 40 bladder cancer patients and 40 controls from teaching hospitals including the Princess Margaret Hospital in Toronto. The epidemiological interview includes an occupational history and some details about possible exposure to industrial chemicals. Twenty-four hour samples of urine are obtained from each subject, the first taken while the patient is at work and the second during the weekend. The urines are concentrated and urinary mutagens are extracted. The Ames/salmonella microsome plate assay is used, using two bacterial strains Ta98 and TA100, with and without S-9 activation. The data analysis is of two main types. The first determines the correlation between the degree of potency of the mutagens in the urine and the type of bladder cancer exhibited by the patient. The analyses also seek to detect a dose-response relationship between urine mutagenicity, degree of invasiveness of the cancer and its biological behaviour. To date we have analysed the data from the urine of 17 patients with bladder tumors and that from 5 controls.

---

[*] RA-201-1.

[**] Assistant Professor, Occupational and Environmental Health Unit, University of Toronto.

[†] OCTRF Research Associate; and Professor of Surgery, U of T.

RELATIONSHIP OF PHEOMELANIN AND PHOTOSENSITIZERS TO SKIN CANCER*

H.F. HABERMAN** and I.A MENON†, *Toronto, Ontario*

This study investigated the role of pheomelanin and ultraviolet (UV) radiation in the etiology of UV-induced skin cancer. The type of melanin in several samples of hair and skin are being correlated with the skin, hair and eye color, minimal erythema dose and family history of skin cancer of volunteers/patients.

Concerning the mechanisms and kinetics of the inflammatory reactions produced by hematoporphyrin and light (used for the photodynamic therapy of cancer), we noted that irradiation of skin sites injected with the drug produced increase in vascular permeability and accumulation of polymorphonuclear leukocytes even under conditions where there was no hemorrhage or erythema. In a further investigation of the mechanism of porphyrin photosensitivity, it was observed during in vitro studies using cell suspension that protoporphyrin phototoxicity was mediated by singlet oxygen, whereas the uroporphyrin cytotoxicity was mediated largely by hydrogen peroxide. In vitro studies in rabbit concerning cutaneous photosensitivity corroborated these findings.

We have developed a rabbit model for the inflammatory reactions produced by PUVA (psoralen and ultraviolet radiation) and have studied the kinetics of the inflammatory process and their variation with changes in the mode of drug administration. We have demonstrated two types of reactions and are investigating mechanisms involved in these reactions and the effects of melanins upon these reactions.

---

* RA-203.

** OCTRF Research Associate; Head of Dermatology, Toronto Western Hospital; and Associate Professor of Medicine, University of Toronto.

† Assistant Professor of Medicine, and of Ophthalmology, U of T.

HORMONE RECEPTOR MECHANISMS IN THE DEVELOPMENT AND TREATMENT OF PROSTATIC NEOPLASIA*

G.E. MOBBS**, *Toronto, Ontario*

A controversial issue in urology is the role of estrogen in the pathophysiology of the prostate, particularly in the development of benign prostatic hyperplasia (BPH). In spite of circumstantial evidence, which suggests that raised estrogen concentrations in plasma and/or prostatic tissue may be associated with BPH in man, no one has yet established a contributory role for estrogen. It has been difficult to demonstrate significant amounts of estrogen receptor (ER) in prostatic tissue; in fact, most studies that used radioligand binding assays (RBA) could detect little or no ER in most BPH specimens.

The recent development of monoclonal antibodies to steroid hormone receptors provides a new method for the quantitation and localization of these proteins in human tissue. We have now investigated the ER and progesterone-receptor (PgR) content of prostatic tissue using these antibodies in enzymeimmunoassays (EIA). With this method, we detected estrogen receptor in all specimens, but in concentrations only marginally higher than the lower limit of detection. Tissue from patients with carcinoma had significantly higher cytosolic ER concentrations than tissue from patients with benign disease. Specimens from estrogen-treated patients had significantly higher nuclear:cytosolic ER ratios than those from untreated patients.

In all known target organs for estrogen, PgR synthesis is induced by estrogen treatment and such synthesis is accepted as a marker for the functional activity of ER. Use of the EIA for PgR in prostatic tissue confirmed the results from radioligand assays: PgR was detected in virtually all specimens, at concentrations higher than those of ER. Carcinoma tissue with a high malignant involvement contained significantly less PgR than benign tissue. Using either method, we observed the highest concentrations of PgR in tissue with little malignant involvement from carcinoma patients treated with estrogen. Overall, the data suggest that, although human prostatic tissue contains only modest amounts of ER, this is in an active form; that is, treatment with estrogen promotes an association between this receptor and the nuclear fraction and it also increases PgR content.

The receptor profile in specimens submitted from untreated patients with carcinoma, but in which no malignant tissue was present, was similar to that of specimens with malignant involvement. Both types of tissue showed some significant differences from BPH specimens. Mean values for cytosolic ER were significantly higher, and those for nuclear PgR were significantly lower than in BPH. This prompts us to speculate that diffuse endocrine changes may occur in malignant prostate glands, which are not limited to overtly malignant areas.

---

* RA-205-1.

** OCTRF Research Associate; and Associate Professor of Surgery (Research), University of Toronto.

In addition to these biochemical studies, we used a monoclonal antibody to PgR to localize this receptor immunohistochemically in benign and malignant prostatic tissue. Progesterone receptor was detected almost exclusively in stromal cells. Except for occasional stained epithelial cells in one benign and one estrogen-treated malignant specimen, both benign and malignant epithelium were negative. The most striking finding was the peracinar arrangement of stained stromal cells in some specimens of glandular BPH, sometimes associated with close juxtaposition of the stained cells with the basement membrane of the acinar epithelium. This finding is of interest in view of current concepts regarding stromal-epithelial interaction.

This project is supported by the National Cancer Institute of Canada.

Windsor Regional Cancer Centre

CLINICAL INVESTIGATIONS

BREAST CANCER

We continue to enter patients into the OCOG Stage I breast cancer trial and also the NCIC MA-4 trial.

We also participate in the OCOG FEC Stage II breast protocol which has escalating levels of chemotherapy using 5-FU, epirubicin and cyclophosphamide.

For advanced breast cancer we have two protocols consisting of:

1. Randomizing patients to high-dose epirubicin versus standard-dose epirubicin in patients who have failed CMF treatment.
2. The use of drolixifene for postmenopausal women who are estrogen-receptor positive and estrogen-receptor unknown.

HODGKIN'S DISEASE

The Windsor Centre participates in the NCIC HD-4 trial in advanced Hodgkin's disease randomizing MOPP-ABV hybrid versus MOPP-ABVD. This is for Stage II and IV Hodgkin's disease.

MULTIPLE MYELOMA

This is the ongoing NCIC MY6 clinical trial.

RECTAL CARCINOMA

We have ethics approval for the NCIC CO4 protocol using pelvic radiation alone versus pelvic radiation plus 5-FU and high-dose leukovorin in completely resected rectal carcinoma.

COLORECTAL CARCINOMA

We are participating in the NCIC CO3 protocol using six cycles of 5-FU and high-dose leukovorin versus no treatment.

HAIRY CELL LEUKEMIA

We are entering patients into the hairy cell leukemia trial randomizing between interferon and pentostatin.

LYMPHOMA

We have received ethics approval for SWOG 8516 trial comparing different regimens – CHOP versus m-BACOD versus ProMace-CytaBOM versus MACOP-B in advanced, high-grade lymphomas.

BRONCHOGENIC CARCINOMA

We have begun a trial at the Centre using short- versus long-course radiation in early unresectable non-small cell lung cancer.

MALIGNANT MELANOMA

We are entering patients into the NCIC ME7 trial using gamma interferon versus levamisole in Stage I or II melanoma

EPIDEMIOLOGY AND STATISTICS

ERRORS IN *CANCER IN ONTARIO* 1988

p. 224	TABLE III	Prostate, column 10 All Ages read 50.3 rather than 50.0
p. 224	TABLE III	for TOTAL read ALL SITES[1]
p. 225	TABLE IV	for ALL SITES read ALL SITES[1]
p. 229	TABLE V	for AGE AT DIAGNOSIS (YEARS) read AGE AT DEATH (YEARS)
p. 230	TABLE VI	for AGE AT DIAGNOSIS (YEARS) read AGE AT DEATH (YEARS)
p. 237	TABLE X	(Continued) Wentworth read 1,162 rather than 1,137
p. 237	TABLE X	(Continued) footnote 2 read … have been expanded by … rather than … have been expand by …

DIVISION OF EPIDEMIOLOGY AND STATISTICS

HEAD OFFICE

Head, and Vice-President OCTRF:
E.A. Clarke, M.B.,B.S.

Cancer Registration Unit:
A. Chiarelli, M.H.Sc.
D. Dale, B.A.Sc.
E.J. Holowaty, M.D.

Statistics Section:
G. Darlington, Ph.D.
G. Fehringer, M.Sc.
G. Hunter, S.R.N.
W. King, M.Sc.
N. Kreiger, Ph.D.
P. Toogood, B.Sc.
H. Weir, M.Sc.

Provincial Programs Unit:
M. Nefsky, M.Sc.
M. Nemes, C.C.H.R.A.(A)

Ontario Breast Screening Program:
C.J. Zylak, M.D.

Epidemiology Research Unit:
I. Fan, B.A.
J. Fleury, B.Sc.
S. Hilditch, M.S.W.
L.D. Marrett, Ph.D.
D. Nishri, M.Sc.
K. Rentner, B.Math
M. Swift, M.Sc.

Senior Epidemiologist:
J. McLaughlin, Ph.D.

During 1989, the activities of the Division of Epidemiology and Statistics have expanded considerably. In May, Dr. E.A. Clarke accepted a part-time contract position with the Ontario Ministry of Health as Provincial Cancer Co-ordinator. Shortly thereafter, Dr. C.J. Zylak of McMaster University and Chedoke-McMaster Hospitals was appointed Director of the new Ontario Breast Screening Program. During the initial phases of its implementation, Mrs. M. Nefsky, Head of the Provincial Programs Unit of the Division, served as Acting Provincial Administrative Co-ordinator. Administered by the Ontario Cancer Treatment and Research Foundation, the Program will be organized and evaluated centrally and operated regionally through the Regional Cancer Centres and the Princess Margaret Hospital.

In 1989, the senior staff of the Division had a retreat to develop a strategic "plan" for the future activities of the Division; this has been extensively discussed and soon will be finalized.

The Cancer Registration Unit continued to work closely with Information Systems on the development of the new Registry database. Several quality control projects have been initiated, including development of a data dictionary and redevelopment of automated edit checking systems for the Registry. The Division is considering the redevelopment of the case resolution system into a true expert system and a pilot project will start shortly to assess the utility of the ARITY PROLOG language.

In 1989, Messrs. W. King and G. Fehringer were appointed to the Statistics Section and Dr. G. Darlington, a senior biostatistician, was recruited to fill a new position created by the OCTRF's Research Advisory Panel.

In response to a growing number of requests, the Statistics Section continued to provide statistical information derived from the Ontario Cancer Registry. These requests come from concerned citizens, health professionals, research workers, health-care facilities, government bodies and scientific agencies. The Epidemiology Research Unit provides a vital link with the University of Toronto and a base for many field studies.

Dr. V.C. Nguyen, epidemiologist for the Northeastern Ontario Oncology Program, serves in the Program and participates in epidemiologic studies with other members of the Division of Epidemiology and Statistics, using Ontario Cancer Registry data. She remains a source of statistical information on cancer incidence and mortality of Northeastern Ontario residents and, in this capacity, answers requests from health-care groups, professionals and nursing students in the region.

Work is nearing completion on the analysis of survival rates for individual cancer sites. Also, the Ontario Cancer Registry is used as the basis for estimating the future burden of cancer in the Province: the staff have made projections of cancer incidence and the number of cases expected to require radiotherapy up to the year 2001.

In addition to the analysis of cancer incidence, survival and mortality in the Province, the staff of the Division contribute to a number of other projects. Using Ontario Cancer Registry data, they collaborate with agencies such as the International Agency for Research on Cancer, the Atomic Energy Control Board of Canada, and the National Cancer Institute in Bethesda, Maryland; also, the staff conduct field studies principally out of the Statistics Section and the Epidemiology Research Unit. These projects receive external support from peer-reviewed grants and contracts.

During 1989, the Division completed a number of research studies. These results were presented to the public through press and TV media, to the first Canadian Conference in Epidemiology held in Ottawa in August and to the National Workshop on Cervical Cancer Screening in November 1989. Grants and contracts were obtained for new studies.

In April 1989, the Annual Seminar in Cancer Epidemiology, organized by the Epidemiology Research Unit, was held with two sessions: one on the primary prevention of cancer and the other on cancer etiology. The speakers at the first session were Drs. G.B. Hill, J. Birdsell and S. Brown and at the second, Drs. W.E. Rawls and L. Ritter. Also in April 1989, the Division hosted the thirteenth semi-annual meeting of the Upstate New York and Southern Ontario Epidemiology Group (UNYSOEG). The staff presented papers relating to various aspects of applied epidemiology during the one-day meeting.

Following this summary of the activities of the Division, we present the most recent data concerning cancer incidence, mortality and treatment in Ontario.

E.A. Clarke, M.B., B.S.
Head, Division of Epidemiology and Statistics and
Vice-President OCTRF

CANCER INCIDENCE, MORTALITY AND TREATMENT IN ONTARIO

The Division of Epidemiology and Statistics is responsible for the reporting of cases and the recording and compilation of data, part of the mandate of the Foundation under the Cancer Act. In pursuit of this objective, the Foundation has maintained and improved a uniform case-recording system, which was adopted by the OCTRF Regional Cancer Centres in 1947 and by the Ontario Cancer Institute incorporating the Princess Margaret Hospital (OCI/PMH) in 1957. The data from the OCTRF Regional Cancer Centres and the OCI/PMH are in machine-readable form from 1960 onwards. In addition to these records, the Foundation's computerized cancer data base contains: individual records on residents of Ontario who died from cancer since 1950; tabulations of deaths by sex, five-year age groups, and type of cancer from 1931 to 1988; individual records of hospital separations describing patients with cancer from 1964 to 1988; and pathology reports on biopsy specimens with cancer from 1972 to 1989. The total volume of the data base, presently almost six million records, provides the Division with a unique opportunity for descriptive cancer epidemiology and allows the Division to assist other cancer researchers in the investigation of possible carcinogenic effects of exposure to occupational and environmental agents.

CANCER INCIDENCE AND MORTALITY

The Ontario Cancer Registry

The Ontario Cancer Registry now has 24 years of incidence data for the Province and comprises information on 602,000 incident cases of cancer diagnosed in residents of Ontario between 1964 and 1987.

The Ontario Cancer Registry employs a unique system of registration, based on computerized record linkage of cancer records collected routinely for other purposes and provided to the Foundation. The Registry receives about 300,000 such records annually. The following province-wide data are routinely forwarded to the Registry:

1. Hospital separations with a mention of cancer collected by the Hospital Medical Records Institute (HMRI) and supplied by the Ontario Ministry of Health: 135,000 computerized records per year.
2. Pathology reports with a mention of cancer submitted voluntarily by hospital pathology laboratories: about 67,000 paper records per year.
3. Reports on patients referred to the OCTRF Regional Cancer Centres and the OCI/PMH: 22,000 computerized records per year.
4. Deaths from all causes supplied by the Registrar General of Ontario: 70,000 computerized records per year.

Once source files are preprocessed, cancer incidence data are created in two major phases. First, the source files are linked in a sequential fashion to bring together all records pertaining to an individual. To link the large volume of data, the Foundation staff have developed a sophisticated, computerized, probabilistic, record-linkage system based on the Generalized Iterative Record Linkage System (GIRLS), designed by Statistics Canada in conjunction with the Epidemiology Unit of the National Cancer Institute of Canada. Then, a set of computerized rules called "case resolution" is applied to the linked records to determine site of disease, histology, and date and method of diagnosis.

The generation of cancer incidence data for Ontario is a joint effort of the staffs of the Division of Epidemiology and Statistics and Information Systems who, together, have developed these systems of record linkage and case resolution.

All incidence data presented here are classified according to the International Classification of Diseases, Ninth Revision (ICD9). Although the Registry had coded cancer sites according to the Eighth Revision of the ICD between 1964 and 1978, all records now have been converted to ICD9.

Cancer Incidence and Mortality, 1987

Because of our efforts to improve the efficiency of the Registry's operation, the frequencies and rates of cancer incidence for 1987, presented in Tables I to IV, are final and not provisional, as they have been for years before 1987 as in previous volumes of *Cancer in Ontario*. Because these data are more complete than those published for previous years, we would caution the reader against making comparisons over time. Available upon request is more complete information describing cancer incidence over the interval 1964 to 1987 including incidence data for smaller geographic areas in the Province (e.g. county) and at the four-digit ICD9 site level. Normally such data can be provided free of charge, within six to eight weeks, following receipt of a written request. We anticipate that provisional incidence data for 1988 will be available by April 1990.

Tables I and II give the frequencies by 5-year age group for each cancer site or group of sites, for males and females respectively, for 1987. The far right-hand column gives rank order to identify sites of most frequent occurrence. The 10 most common sites, in terms of their sex-specific incidence frequencies, are shown in Fig. 1 with cancer mortality data for 1987.

Tables III and IV present incidence and mortality rates by age group and site, for males and females respectively, for 1987. In these two tables, the rates for 15-year age groups and for all ages are age-adjusted, using the world standard population shown in Table VII.

The method of direct age-adjustment used here is described by Waterhouse et al in *Cancer Incidence in Five Continents*, vol. 5. Rates in the tables have been "age-adjusted" to assist comparisons between the different areas in the world. Age adjustment allows us to account for differences caused solely by differences in age distribution in these areas. The rates in Tables III and IV can be compared with any other rates covering the same age span and using the same standard population for adjustment.

TABLE I

Annual Number of New Cases of Malignant Neoplasms in Males, by Site of Disease and Age at Diagnosis, Ontario 1987

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DIAGNOSIS (YEARS)																		RANK[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	Age Unknown	All Ages	
Lip and oral cavity	140-145	1	1	0	4	6	4	9	17	14	31	43	67	85	89	71	124	4	570	8
Pharynx	146-148	1	0	0	0	2	2	4	4	9	14	18	38	37	26	23	20	0	198	
Esophagus	150	0	0	0	0	0	3	1	3	3	17	14	43	57	39	45	66	1	292	
Stomach	151	0	0	0	0	0	1	6	6	12	20	40	57	84	127	121	194	1	669	7
Intestine, except rectum	152, 153	0	0	0	3	5	8	4	15	29	68	100	196	276	298	305	565	3	1,875	3
Rectum and anus	154	0	0	0	0	1	1	3	11	19	28	50	115	131	160	158	204	2	883	5
Pancreas	157	0	0	0	0	0	0	0	7	6	13	39	39	54	63	93	140	0	454	
Nasal cavities, middle ear and accessory sinuses	160	0	0	0	1	0	1	3	1	1	3	3	4	5	4	8	13	0	47	
Larynx	161	0	0	0	0	0	0	0	3	9	13	34	50	71	56	46	52	2	336	
Trachea, bronchus and lung	162	0	0	0	0	1	2	6	20	50	96	243	453	669	683	625	862	7	3,717	1
Bone	170	1	4	10	6	4	6	7	5	2	4	1	5	5	5	5	2	0	72	
Connective tissue	171	4	1	2	6	3	9	9	9	5	7	8	16	10	10	9	25	1	134	
Malignant melanoma of skin	172	0	2	3	0	9	25	38	42	45	50	39	63	70	42	45	62	5	540	10
Prostate	185	1	0	0	0	0	0	2	1	0	10	41	153	365	584	708	1,356	8	3,229	2
Testis	186	1	0	1	12	49	46	50	30	25	10	3	4	2	3	2	5	0	243	
Bladder	188	0	0	0	0	2	6	6	20	28	44	87	126	181	222	229	426	2	1,379	4
Kidney and other urinary	189	16	2	0	0	1	4	4	13	20	28	49	60	80	88	97	107	0	569	9
Brain and other nervous system	191, 192	12	10	9	6	11	18	18	18	34	27	21	44	39	56	38	33	0	394	
Thyroid gland	193	0	0	1	4	2	11	14	7	7	6	12	7	8	7	7	6	0	99	
Lymphosarcoma and reticulosarcoma	200	4	3	2	6	5	8	14	16	14	28	31	40	47	35	72	72	0	397	
Hodgkin's disease	201	0	2	3	16	26	25	12	20	11	8	5	10	10	9	9	9	0	175	
Other lymphomas	202	2	1	1	3	6	3	10	20	30	28	29	41	43	41	42	49	0	349	
Multiple myeloma	203	0	0	0	0	0	0	0	0	3	11	14	18	21	43	44	81	0	235	
Leukemia	204-208	38	13	9	12	15	12	8	9	11	21	46	47	60	88	100	187	4	680	6
Other and non-specific	Residual	20	1	5	3	8	18	20	21	28	45	70	118	195	191	216	368	14	1,341	
TOTAL	140-208[3]	101	40	46	82	156	213	248	318	415	630	1,040	1,814	2,605	2,969	3,118	5,028	54	18,877	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for 10 most common sites (or site groups).

[3] Excluding non-melanotic skin cancers (ICD9 number 173).

TABLE II

Annual Number of New Cases of Malignant Neoplasms in Females, by Site of Disease and Age at Diagnosis, Ontario 1987

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DIAGNOSIS (YEARS)																		RANK[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	Age Unknown	All Ages	
Lip and oral cavity	140-145	1	0	2	3	3	5	4	4	5	8	9	27	29	29	42	80	0	251	
Pharynx	146-148	0	0	0	1	1	1	1	4	4	4	7	15	11	18	7	12	0	86	
Esophagus	150	0	0	0	0	0	0	0	0	2	5	4	9	16	18	16	39	0	109	
Stomach	151	0	0	0	0	1	0	3	4	5	7	15	43	51	45	46	166	1	387	
Intestine, except rectum	152, 153	0	1	0	0	2	6	10	14	31	64	103	161	232	276	289	803	1	1,993	2
Rectum and anus	154	1	1	0	0	2	3	2	13	17	22	24	63	74	98	99	211	3	633	6
Pancreas	157	0	0	1	0	1	2	1	8	6	8	19	25	46	62	76	178	0	433	
Nasal cavities, middle ear and accessory sinuses	160	0	0	0	1	0	0	0	1	1	0	4	2	4	8	4	10	0	35	
Larynx	161	0	0	0	0	0	0	0	4	2	6	3	15	11	8	12	13	0	74	
Trachea, bronchus and lung	162	0	0	0	0	0	5	8	13	47	83	146	203	276	302	254	414	4	1,755	3
Bone	170	4	2	3	5	2	2	1	3	4	4	4	4	2	6	2	4	0	52	
Connective tissue	171	2	1	3	5	5	2	7	2	9	5	4	12	3	10	7	29	0	106	
Malignant melanoma of skin	172	0	1	1	3	18	36	60	49	56	49	46	43	56	40	41	86	4	589	7
Breast	174	0	0	1	1	2	32	98	229	343	402	452	480	587	553	494	959	7	4,640	1
Cervix uteri	180	0	0	0	1	8	41	53	76	73	42	36	46	57	44	27	61	1	566[3]	8
Body of uterus	182	0	0	0	0	0	0	11	14	28	60	85	123	206	194	144	180	3	1,048	4
Other and unspecified uterus	179, 181	0	0	0	1	1	1	1	2	4	3	3	3	4	5	2	11	0	41	
Ovary and fallopian tube	183	0	1	1	4	9	19	22	29	32	52	64	70	103	86	90	156	0	738	5
Bladder	188	0	0	0	1	3	6	7	7	5	13	27	47	56	49	67	175	1	464	10
Kidney and other urinary	189	10	0	0	0	0	2	7	10	13	25	33	40	48	60	51	90	0	389	
Brain and other nervous system	191, 192	14	8	10	4	3	15	14	11	9	17	26	30	40	22	38	55	0	316	
Thyroid gland	193	1	2	3	8	13	37	34	34	34	24	23	21	19	22	13	16	0	304	
Lymphosarcoma and reticulosarcoma	200	1	1	1	6	3	5	3	9	4	11	21	27	40	48	43	83	0	306	
Hodgkin's disease	201	0	3	3	11	29	25	12	6	11	3	3	5	6	6	5	15	0	143	
Other lymphomas	202	1	3	0	2	2	10	6	13	9	20	25	30	29	29	31	80	2	292	
Multiple myeloma	203	0	0	0	0	0	0	2	0	1	1	13	22	38	20	37	75	0	209	
Leukemia	204-208	29	17	4	9	10	7	8	12	13	16	16	18	39	55	61	201	1	516	9
Other and non-specific	Residual	16	5	1	1	10	12	12	20	26	40	57	84	128	149	171	499	5	1,236	
TOTAL	140-208[4]	80	46	34	67	128	274	387	591	794	994	1,272	1,668	2,211	2,262	2,169	4,701	33	17,711	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for 10 most common sites (or site groups).

[3] Approximately 10% non-invasive cancer of the cervix.

[4] Excluding non-melanotic skin cancers (ICD9 number 173).

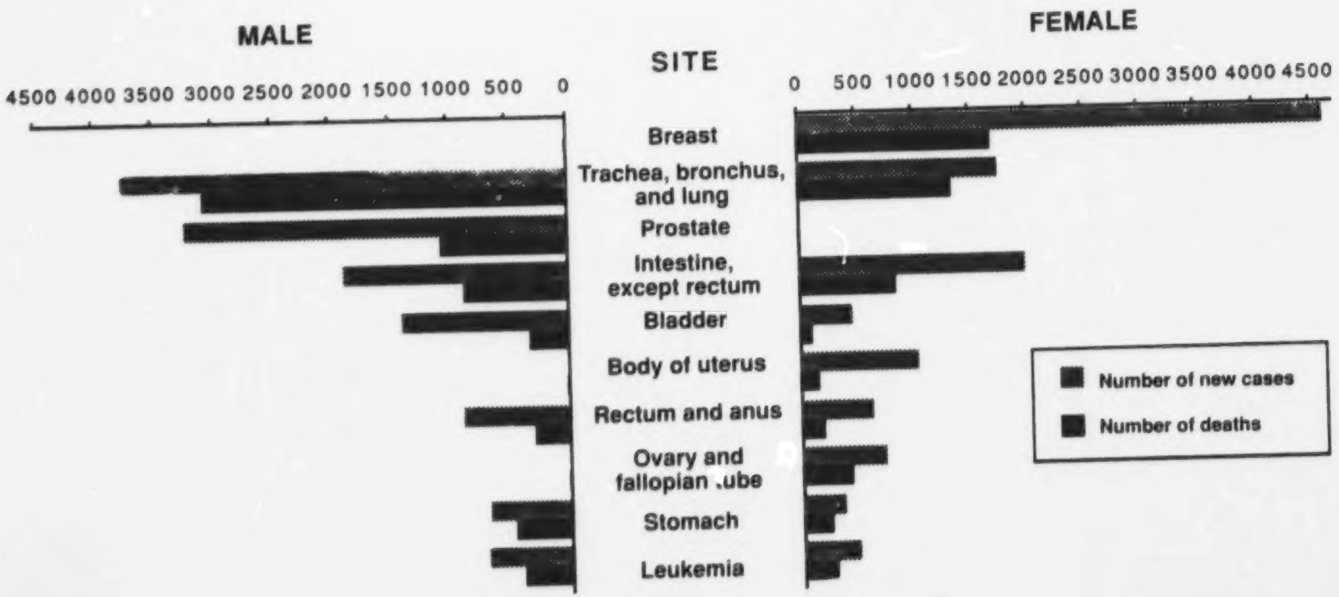


Fig. 1 New cases of, and deaths due to, malignant neoplasms, by sex and site of disease, for common cancers, Ontario 1987.

TABLE III

Age-adjusted Rates[1] and Cumulative Risks (age 0-74)[2], Incidence (I) and Mortality (M) from Malignant Neoplasms in Males, by Site and Age, Ontario 1987

SITE OF DISEASE	ICD9[3] NUMBER	INCIDENCE/ MORTALITY	AGE AT DIAGNOSIS/DEATH (YEARS)							
			0-14	15-29	30-44	45-59	60-74	75+	All Ages	0-74
Lip and oral cavity	140-145	I	0.2	1.2	3.8	19.0	50.2	85.7	10.1	1.16
		M	0.0	0.0	0.3	4.1	13.8	20.9	2.4	0.28
Pharynx	146-148	I	0.1	0.3	1.7	9.3	17.7	13.1	3.7	0.45
		M	0.1	0.0	0.8	3.6	9.0	6.4	1.7	0.20
Esophagus	150	I	0.0	0.2	0.7	9.8	28.9	45.6	5.2	0.62
		M	0.0	0.0	0.2	9.6	25.6	38.6	4.5	0.53
Stomach	151	I	0.0	0.1	2.3	15.6	67.2	140.6	11.6	1.39
		M	0.0	0.0	1.5	10.8	38.7	104.7	7.5	0.82
Intestine, except rectum	152, 153	I	0.0	1.3	4.8	48.1	178.6	395.9	32.4	3.68
		M	0.0	0.2	3.2	16.1	78.7	222.0	14.6	1.59
Rectum and anus	154	I	0.0	0.2	3.3	25.1	91.1	139.4	15.4	1.93
		M	0.0	0.1	0.7	6.9	28.1	77.1	5.3	0.59
Pancreas	157	I	0.0	0.0	1.3	12.2	42.1	93.7	7.7	0.93
		M	0.1	0.1	1.0	11.7	49.0	101.9	8.5	1.00
Larynx	161	I	0.0	0.0	1.2	12.8	35.6	34.6	6.0	0.77
		M	0.0	0.0	0.1	3.8	12.7	25.9	2.3	0.27
Trachea, bronchus and lung	162	I	0.0	0.2	7.6	103.3	403.6	579.7	64.8	7.90
		M	0.0	0.0	5.4	75.9	327.1	553.1	52.9	6.32
Bone	170	I	1.4	1.4	1.3	1.4	3.1	1.2	1.5	0.13
		M	0.3	1.0	0.3	0.1	2.5	2.3	0.7	0.07
Malignant melanoma of skin	172	I	0.5	2.6	11.9	20.9	32.3	42.2	9.8	1.03
		M	0.0	0.5	2.4	3.8	7.2	12.8	2.0	0.22
Prostate	185	I	0.1	0.0	0.3	25.4	332.4	947.5	52.8	5.94
		M	0.0	0.0	0.0	5.2	69.2	401.4	15.0	1.32
Testis	186	I	0.2	8.6	9.7	2.5	1.4	3.0	4.5	0.34
		M	0.0	0.2	0.5	0.5	0.2	0.0	0.2	0.02
Bladder	188	I	0.0	0.6	5.3	34.3	127.9	300.4	23.8	2.69
		M	0.0	0.0	0.2	2.5	24.3	95.1	4.5	0.45
Kidney and other urinary	189	I	2.1	0.4	3.6	18.5	53.7	74.8	10.5	1.25
		M	0.0	0.0	1.0	7.1	22.8	38.4	4.1	0.48
Brain and other nervous system	191, 192	I	3.2	2.9	6.8	12.5	27.2	22.6	7.7	0.81
		M	0.9	1.1	3.5	10.6	18.3	17.3	4.7	0.51
Thyroid gland	193	I	0.1	1.4	2.6	3.5	4.5	3.7	1.8	0.19
		M	0.0	0.0	0.0	0.7	1.3	1.3	0.2	0.03
Lymphosarcoma and reticulosarcoma	200	I	1.0	1.6	4.2	13.6	30.9	49.2	7.2	0.83
		M	0.0	0.4	0.8	1.7	6.1	15.7	1.3	0.14
Hodgkin's disease	201	I	0.5	5.6	4.0	3.2	5.7	6.0	3.4	0.29
		M	0.0	0.4	1.5	1.0	2.9	2.8	0.8	0.09
Other lymphomas	202	I	0.4	1.0	5.9	13.4	25.7	31.8	6.4	0.72
		M	0.0	0.2	1.6	6.5	22.5	49.0	4.3	0.50
Multiple myeloma	203	I	0.0	0.0	0.3	5.9	21.7	57.4	4.0	0.46
		M	0.0	0.0	0.4	3.4	15.6	39.1	2.8	0.32
Leukemia	204-208	I	6.6	3.3	2.7	15.5	49.9	128.8	12.7	1.26
		M	2.2	2.0	2.4	7.8	27.7	84.4	6.9	0.67
ALL SITES[4]	140-208[4]	I	20.0	37.0	94.4	462.1	1762.9	3481.6	330.1	31.90
		M	4.2	7.0	31.1	217.8	902.2	2173.3	166.0	17.06

[1] Age-adjusted by the direct method to the World Standard Population (See Table VII), expressed per 100,000 persons.

[2] Cumulative risk approximate to the percent probability of a cancer diagnosis/death occurring by age 74 (Reference: Day NE. International Agency for Research on Cancer (IARC) Scientific Publication No. 15, pp. 443-52, 1976).

[3] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[4] Excluding non-melanotic skin cancers (ICD9 number 173). Note that any individual sites not specifically included in the table are included in "ALL SITES".

TABLE IV

Age-adjusted Rates[1] and Cumulative Risks (age 0-74)[2], Incidence (I) and Mortality (M) from Malignant Neoplasms in Females, by Site and Age, Ontario 1987

SITE OF DISEASE	ICD9[3] NUMBER	INCIDENCE/ MORTALITY	AGE AT DIAGNOSIS/DEATH (YEARS)							
			0-14	15-29	30-44	45-59	60-74	75+	All Ages	0-74
Lip and oral cavity	140-145	I	0.3	0.9	1.2	5.7	16.8	31.3	3.5	0.41
		M	0.0	0.0	0.2	1.5	4.3	8.6	0.8	0.09
Pharynx	146-148	I	0.0	0.3	0.9	3.4	6.3	4.8	1.4	0.17
		M	0.0	0.0	0.0	0.5	0.8	1.9	0.2	0.02
Esophagus	150	I	0.0	0.0	0.2	2.4	8.6	15.0	1.5	0.18
		M	0.0	0.0	0.0	2.1	7.6	20.2	1.4	0.15
Stomach	151	I	0.0	0.1	1.1	8.2	24.4	64.0	4.9	0.54
		M	0.0	0.1	1.0	7.0	19.7	48.0	4.0	0.46
Intestine, except rectum	152, 153	I	0.1	0.6	5.3	43.7	135.0	309.8	26.0	2.92
		M	0.0	0.1	2.0	15.3	55.1	150.7	10.7	1.16
Rectum and anus	154	I	0.2	0.4	3.1	14.2	45.8	80.9	8.6	1.02
		M	0.0	0.0	0.3	3.7	15.9	37.6	2.8	0.33
Pancreas	157	I	0.1	0.2	1.4	6.9	30.7	68.3	5.5	0.65
		M	0.0	0.0	0.8	7.4	25.4	85.3	5.2	0.56
Larynx	161	I	0.0	0.0	0.6	3.1	5.3	5.0	1.2	0.14
		M	0.0	0.0	0.1	0.6	2.2	3.0	0.4	0.04
Trachea, bronchus and lung	162	I	0.0	0.4	6.8	57.8	143.0	161.3	26.1	3.20
		M	0.0	0.1	4.0	38.8	109.0	123.5	18.8	2.37
Bone	170	I	1.0	0.8	0.8	1.7	1.7	1.6	1.1	0.09
		M	0.1	0.3	0.0	0.0	0.9	1.2	0.2	0.02
Malignant melanoma of skin	172	I	0.2	4.5	15.2	19.4	23.8	33.1	9.6	0.95
		M	0.0	0.1	1.4	3.0	5.0	4.2	1.3	0.15
Breast	174	I	0.1	2.7	64.7	184.6	281.9	372.4	72.9	7.84
		M	0.0	0.5	16.1	62.1	106.3	187.9	25.7	2.81
Cervix uteri	180	I	0.0	3.8	18.9	17.2	22.6	23.0	9.4	0.93
		M	0.0	0.4	2.2	6.1	10.4	13.5	2.6	0.29
Other uterus	179, 181, 182	I	0.0	0.3	5.8	37.3	96.6	74.3	16.9	2.11
		M	0.0	0.1	0.2	2.0	15.9	27.9	2.3	0.28
Ovary and other uterine adnexa	183	I	0.2	2.6	7.8	25.6	48.0	60.9	11.5	1.29
		M	0.0	0.3	2.1	13.5	37.1	49.8	6.8	0.83
Bladder	188	I	0.0	0.8	1.7	11.4	29.1	68.1	6.2	0.69
		M	0.0	0.0	0.2	0.9	5.7	27.3	1.2	0.12
Kidney and other urinary	189	I	1.2	0.2	2.8	13.4	27.2	35.5	6.1	0.69
		M	0.0	0.0	0.4	2.6	9.7	22.4	1.8	0.20
Brain and other nervous system	191, 192	I	3.5	1.8	3.1	9.9	17.1	21.7	5.6	0.55
		M	0.9	0.7	1.8	6.5	16.3	16.3	3.6	0.42
Thyroid gland	193	I	0.6	4.7	9.4	9.6	9.4	6.1	5.5	0.51
		M	0.0	0.0	0.1	0.3	1.8	4.1	0.3	0.04
Lymphosarcoma and reticulosarcoma	200	I	0.3	1.3	1.5	7.9	22.4	32.5	4.5	0.52
		M	0.1	0.1	0.3	2.0	5.1	7.8	1.0	0.12
Hodgkin's disease	201	I	0.6	5.4	2.7	1.5	2.9	5.9	2.6	0.20
		M	0.0	0.3	0.5	0.9	1.1	3.1	0.5	0.04
Other lymphomas	202	I	0.4	1.1	2.6	10.3	15.2	31.2	4.4	0.46
		M	0.1	0.3	0.8	4.7	12.7	26.7	2.6	0.30
Multiple myeloma	203	I	0.0	0.0	0.3	4.6	16.2	28.6	2.8	0.34
		M	0.0	0.0	0.1	3.1	12.8	23.6	2.1	0.26
Leukemia	204-208	I	5.8	2.3	3.1	6.9	26.0	77.3	7.8	0.69
		M	1.4	1.2	1.6	5.0	13.8	40.0	3.8	0.36
ALL SITES[4]	140-208[4]	I	18.0	38.1	168.6	534.5	1,137.5	1,818.4	264.4	25.56
		M	3.4	5.3	39.1	205.6	553.2	1,111.0	122.2	12.09

[1] Age-adjusted by the direct method to the World Standard Population (See Table VII), expressed per 100,000 persons.

[2] Cumulative risk approximate to the percent probability of a cancer diagnosis/death occurring by age 74 (Reference: Day NE. International Agency for Research on Cancer (IARC) Scientific Publication No. 15.

[3] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977. pp. 443-52. 1976).

[4] Excluding non-melanotic skin cancers (ICD9 number 173). Note that any individual sites not specifically included in the table are included in "ALL SITES".

The "cumulative risk" (0-74) shown in the final column of Tables III and IV is described in detail in *Cancer Incidence in Five Continents*. Expressed per 100, it is a reasonable approximation to the risk (to age 74) of being diagnosed with, or dying of, the given cancer. Thus, if the current age-specific rates for female lung cancer were to remain unchanged throughout her life, a female born in 1987 would have about a 3% chance of being diagnosed with lung cancer by age 74. Of course, if age-specific rates continue to rise, the cumulative risk will increase also.

Cancer Mortality, 1988

The most current cancer mortality data are for 1988; these were provided by the Office of the Registrar General of Ontario. Figs. 2 and 3 show the frequencies of death due to malignant neoplasms of all types, relative to other major groups of causes of death among males and females. Tables V and VI give the numbers of cancer deaths by age group at death and site; the same format and groupings are used in Tables I and II for cancer incidence.

Populations

Table VII shows sex- and age-specific population data for Ontario for the years 1987 and 1988 and for the "world standard". This table provides the 1987 and the 1988 Ontario population (post-censal estimates) for those who wish to calculate age-specific cancer incidence and mortality rates from data given in the previous sections. The world population is an artificial standard, frequently used in the calculation of age-adjusted rates. The Ontario population data are provided by Statistics Canada and the world population is taken from *Cancer Incidence in Five Continents*.

CANCER TREATMENT

Hospital Caseload

During the Ontario Ministry of Health's fiscal year 1987-88, active and rehabilitation hospitals in Ontario reported 75,707 separations (discharges and deaths), in which the primary diagnosis was cancer. These accounted for 5.7% of all hospital separations and 1,123,434 days of hospital care. The average length of stay for cancer patients declined from 16.9 days in 1972 to 14.8 days in 1987-88*.

New Cancer Registrations

In the last decade (1979-1988), the number of new cases (a patient presenting with a case of cancer not previously registered at any centre) registered at the OCTRF Regional Cancer Centres and the OCI/PMH has increased by 48.6% from 16,305 to 24,222 (Table VIII). The distribution by centre of the numbers of in situ lesions,

---

*Hospital statistics 1987-1988 published by the Ontario Ministry of Health.

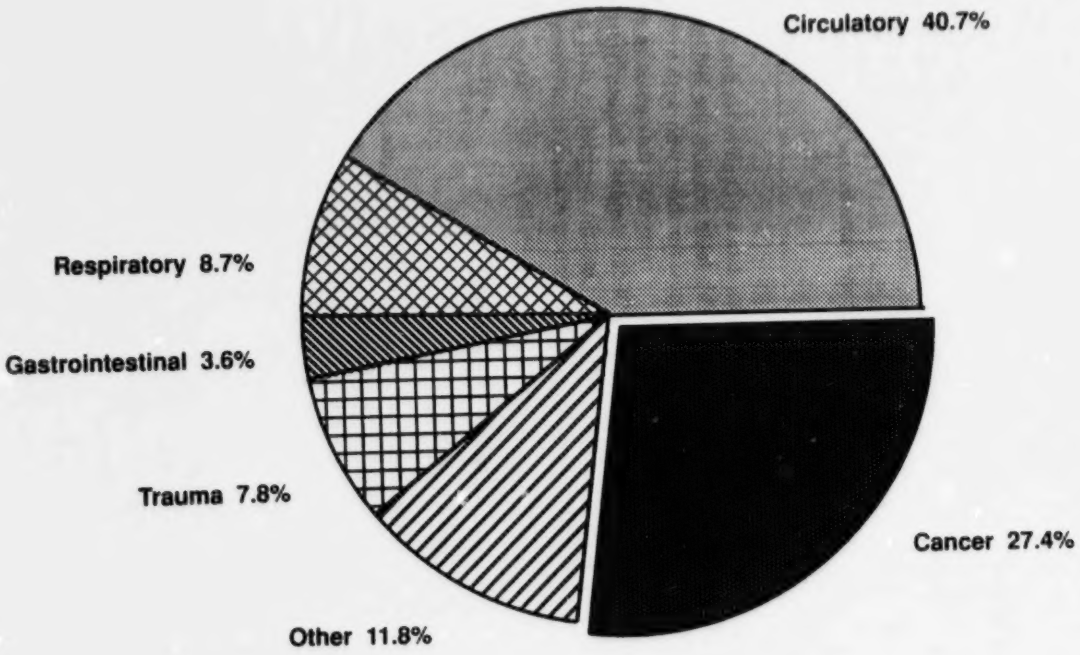


Fig. 2 Percentage distribution of major causes of death in males, Ontario 1988.

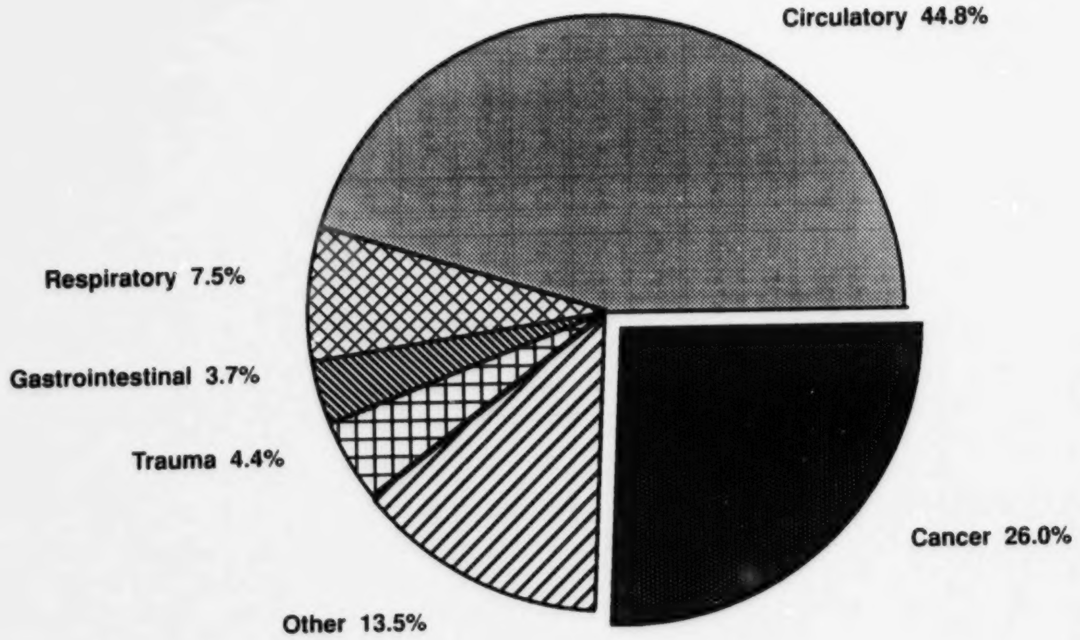


Fig. 3 Percentage distribution of major causes of death in females, Ontario 1988.

TABLE V

Number of Deaths due to Malignant Neoplasms in Males, by Site of Disease and Age at Death, Ontario 1988

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DEATH (YEARS)																	RANK[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	All Ages	
Lip and oral cavity	140-145	0	0	0	0	1	1	2	0	2	6	9	17	23	24	22	35	142	
Pharynx	146-148	0	0	1	1	0	1	0	0	1	3	9	14	18	16	13	9	86	
Esophagus	150	0	0	0	0	0	0	1	1	5	13	20	49	52	51	45	68	305	8
Stomach	151	0	0	0	0	0	0	4	3	8	16	17	29	52	64	81	195	469	4
Intestine, except rectum	152, 153	0	0	0	0	0	0	2	7	4	30	41	57	113	157	153	333	897	3
Rectum and anus	154	0	0	0	0	0	1	0	1	3	6	10	18	33	59	46	104	281	10
Pancreas	157	0	0	0	0	0	0	1	6	12	12	18	41	62	83	81	150	466	5
Nasal cavities, middle ear and accessory sinuses	160	0	1	0	0	0	0	1	1	1	1	0	0	0	1	1	7	14	
Larynx	161	0	0	0	0	0	0	0	0	0	5	7	19	37	23	20	39	150	
Trachea, bronchus and lung	162	0	0	0	0	0	2	2	13	38	82	167	323	562	642	540	886	3,257	1
Bone	170	0	3	1	2	1	1	1	1	1	2	1	2	1	2	0	0	19	
Connective tissue	171	1	0	1	0	2	4	3	2	2	1	0	0	2	9	6	11	44	
Malignant melanoma of skin	172	0	0	0	0	1	3	4	10	7	10	6	20	8	21	9	17	116	
Breast	175	0	0	0	0	0	0	0	1	0	0	0	2	3	0	1	2	9	
Prostate	185	0	0	0	0	0	0	0	0	0	3	9	22	82	118	216	637	1,087	2
Testis	186	0	0	0	2	3	6	2	2	0	1	1	0	0	2	2	3	24	
Bladder	188	0	0	0	0	0	0	0	1	4	1	6	12	32	31	56	170	313	7
Kidney and other urinary	189	0	1	0	0	1	0	1	2	8	12	17	17	33	36	34	79	241	
Brain and other nervous system	191, 192	6	5	5	2	4	4	9	17	12	18	22	34	40	53	22	42	295	9
Thyroid gland	193	0	0	0	0	0	0	0	0	0	1	1	0	1	1	3	2	9	
Lymphosarcoma and reticulosarcoma	200	0	0	2	0	1	2	0	1	2	2	4	6	5	4	9	12	50	
Hodgkin's disease	201	0	0	0	0	7	6	1	4	2	2	2	4	4	6	6	2	46	
Other lymphomas	202	1	1	0	1	4	3	7	12	12	10	17	29	32	39	40	67	275	
Multiple myeloma	203	0	0	0	0	0	0	0	0	2	3	4	7	24	33	25	52	150	
Leukemia	204-208	4	5	2	2	6	4	4	7	5	15	22	24	34	46	65	155	400	6
Other and non-specific	Residual	3	3	1	1	5	1	5	7	15	27	47	109	159	200	174	362	1,119	
TOTAL	140-208[3]	15	19	13	11	36	39	50	99	146	282	457	855	1,412	1,721	1,670	3,439	10,264	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for sites with more than 100 deaths.

[3] Omitted are 43 deaths due to non-melanotic cancer of the skin (ICD9 number 173).

TABLE VI

Number of Deaths due to Malignant Neoplasms in Females, by Site of Disease and Age at Death, Ontario 1988

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DEATH (YEARS)																	RANK[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	All Ages	
Lip and oral cavity	140-145	0	0	0	0	0	1	0	2	3	1	2	7	11	9	11	19	66	
Pharynx	146-148	0	0	0	0	0	0	1	0	0	0	3	0	5	3	6	8	26	
Esophagus	150	0	0	0	0	0	0	1	0	4	2	2	5	10	21	19	56	120	
Stomach	151	0	0	0	0	0	0	0	5	5	4	14	15	22	30	37	126	258	7
Intestine, except rectum	152, 153	0	0	0	0	0	1	4	2	9	28	43	48	85	108	128	424	880	3
Rectum and anus	154	0	0	0	0	0	1	0	3	1	7	2	14	24	33	26	95	206	10
Pancreas	157	0	0	0	0	0	0	0	0	3	7	8	31	44	84	55	206	438	5
Nasal cavities, middle ear and accessory sinuses	160	0	1	0	0	0	0	0	0	0	0	0	1	0	4	0	6	12	
Larynx	161	0	0	0	0	0	0	0	0	0	0	1	4	5	2	3	8	23	
Trachea, bronchus and lung	162	0	0	0	0	0	1	3	9	31	52	96	169	190	284	252	396	1,483	2
Bone	170	0	2	0	3	1	0	0	1	0	0	0	1	4	0	0	2	14	
Connective tissue	171	0	2	0	2	1	3	1	1	0	1	2	1	2	1	5	10	32	
Malignant melanoma of skin	172	0	0	0	0	1	3	6	1	5	4	4	10	8	8	8	13	71	
Breast	174	0	0	0	0	0	5	23	46	79	113	123	205	231	203	195	487	1,710	1
Cervix uteri	180	0	0	0	0	1	5	6	14	18	9	10	18	17	23	33	40	194	
Other uterus	179, 181, 182	0	0	0	0	0	0	1	1	0	2	2	11	16	30	27	82	172	
Ovary and fallopian tube	183	0	0	0	0	1	2	8	5	14	17	21	60	78	67	65	122	460	4
Bladder	188	0	0	0	0	0	0	0	2	0	1	3	3	13	13	20	95	150	
Kidney and other urinary	189	1	0	0	0	0	1	1	0	2	7	6	8	12	24	13	69	144	
Brain and other nervous system	191, 192	5	3	4	2	2	5	4	6	10	9	15	14	36	23	24	46	208	9
Thyroid gland	193	0	0	0	0	0	0	0	0	0	1	1	1	0	6	2	13	24	
Lymphosarcoma and reticulosarcoma	200	1	0	0	1	0	2	1	0	1	2	0	3	5	1	7	17	41	
Hodgkin's disease	201	0	0	0	2	2	3	1	4	2	0	0	3	0	1	2	5	25	
Other lymphomas	202	1	0	0	1	2	4	4	3	12	5	11	14	12	38	34	95	236	8
Multiple myeloma	203	0	0	0	0	0	0	0	0	0	0	4	12	23	22	29	59	149	
Leukemia	204-208	4	1	4	5	7	3	4	5	12	14	11	13	21	39	47	138	328	6
Other and non-specific	Residual	7	0	0	1	1	1	4	8	11	25	43	60	124	138	175	474	1,072	
TOTAL	140-208[3]	19	9	8	17	19	41	73	118	222	311	427	731	998	1,215	1,223	3,111	8,542	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for sites with more than 100 deaths.

[3] Omitted are 16 deaths due to non-melanotic cancer of the skin (ICD9 number 173).

TABLE VII

World Standard Population and Estimated Population 1987 and 1988, of Ontario (In Thousands)

AGE GROUP	WORLD STANDARD[1]	ONTARIO, 1987[2]		ONTARIO, 1988[2]	
	MALE OR FEMALE	MALE	FEMALE	MALE	FEMALE
0-4	12.0	332.4	316.0	338.7	322.9
5-9	10.0	315.8	301.4	323.1	308.1
10-14	9.0	321.9	305.8	320.7	305.6
15-19	9.0	353.6	335.3	353.9	334.5
20-24	8.0	403.1	397.0	393.6	383.4
25-29	8.0	419.3	425.3	432.3	434.7
30-34	6.0	387.2	402.7	401.2	413.5
35-39	6.0	362.0	371.8	366.0	377.5
40-44	6.0	316.0	316.8	332.5	334.2
45-49	6.0	252.5	252.2	263.5	263.7
50-54	5.0	231.2	230.6	231.5	232.0
55-59	4.0	227.8	230.5	228.3	230.6
60-64	4.0	204.5	228.0	207.4	228.7
65-69	3.0	160.5	192.1	168.7	202.7
70-74	2.0	119.4	153.5	118.9	153.4
75-79	1.0	78.7	115.6	82.3	119.5
80-84	0.5	42.4	77.4	43.9	79.9
85+	0.5	25.4	65.1	26.7	67.9
TOTAL	100.0	4,553.7	4,717.1	4,633.3	4,792.8

[1] Waterhouse, John et al (eds), Cancer Incidence in Five Continents, Vol V. World Health Organization, Geneva, 1987, p.792.

[2] Source: Statistics Canada.

neoplasms of uncertain behaviour and multiple skin cancers is shown at the foot of Table IX.

This increase in the number of cases seen at the OCTRF Regional Cancer Centres can be attributed in part to the greater occurrence of cancer in the population during the last decade. This increase represents a combination of an increase in population in Ontario, which is also aging, and an increase in smoking-related cancers. It is anticipated that these trends will continue with an expected annual increase in the absolute number of new cases of cancer requiring treatment.

In Table IX, for 1988, the major sites of newly registered cancers at the OCTRF Regional Cancer Centres were lung, bronchus and trachea (15.2%), and breast (19.1%), followed by non-melanoma of the skin (8.4%). Of the 22,361 cancers seen for the first time at one of the OCTRF Regional Cancer Centres or the OCI/PMH, 15.9% were seen in Hamilton, 5.1% in Kingston, 13.% in London, 13.8% in Ottawa, 2.2% in Sudbury, 2.5% in Thunder Bay, 14.4% at Toronto-Bayview, 4.8% in Windsor, and 28.3% at the Princess Margaret Hospital.

It should be noted that a "new case" registered at an OCTRF Regional Cancer Centre refers to a case of cancer seen for the first time during that year at any one of the centres. If a case is seen at two centres in the same year, the case is recorded as seen only by the first centre (2.6% of cases were seen at more than one centre in the same year).

The location of the peripheral clinics associated with the OCTRF Regional Cancer Centres and the OCI/PMH, and the type of outreach program, determine the referral pattern to each (Table X). Thus, in Lambton County, of the 320 cases resident in the county, 312 were referred to the London Centre and only a small number to other centres. On the other hand, in Halton Regional Municipality, of the 629 cases resident in that area, 386 were referred to the Hamilton Centre, 211 to OCI/PMH and 26 were referred to the Toronto-Bayview Centre. From the Province of Quebec, 504 residents were referred to OCTRF Regional Cancer Centres; most were seen at the Ottawa Centre. An additional 198 residents of other provinces were seen in Ontario, principally at the OCI/PMH. Of the 165 residents of the USA and other countries treated in Ontario, most were seen at the OCI/PMH, and the Toronto-Bayview and Ottawa Centres.

The data in Tables VIII-X were extracted from the OCTRF Regional Cancer Centres in August 1989. Data extracted later may differ slightly from those presented here.

ACKNOWLEDGEMENTS

We acknowledge with gratitude the continuing co-operation of government. The Ontario Ministry of Health has provided source records and advice; the Office

of the Registrar General of the Ministry of Consumer and Commercial Relations has provided computerized data on deaths due to all causes in Ontario residents and, in addition, has provided facilities for an on-site search of their records for treatment evaluation and other research. We appreciate the assistance of the staff of the Hospital Medical Records Institute (HMRI) and are indebted to the medical records staff of all hospitals in Ontario who willingly and promptly provide additional information, primarily for the generation of incidence data, but also to ensure the high quality of data entered in the Ontario Cancer Registry.

We extend special thanks to the Chief Operating Officers of the OCTRF Regional Cancer Centres and the OCI/PMH and their managers of health records for support during the year, and to the members of the Foundation's Standing Committee on Records and Statistics and its sub-committees.

We acknowledge with gratitude the assistance of all the staff of Information Systems in the processing of the Foundation's large data base. In particular, we thank the individuals working under the direction of Messrs. Rob Belsey and Tom Broz.

Our special thanks are extended to Mrs. Mary Nemes, Manager of Provincial Programs Unit in the Division, Miss Darlene Dale, Manager of Operations, Cancer Registration Unit, and the staff of the Division for their dedication to the generation of incidence data and their continual effort to improve the quality of the Ontario Cancer Registry. We are also grateful to Dr. Van C. Nguyen who, with the help of Janice Fleury, Jean Rowan and Collette Hill, prepared this report.

TABLE VIII

New Cancer Cases Registered by Treatment Centre, 1979-1988[1,2]

CENTRE	YEAR OF REGISTRATION									
	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988[3]
Hamilton	2,594	2,507	2,537	2,688	2,780	2,782	3,498	3,472	3,729	3,849
Kingston	999	984	997	1,073	1,226	1,195	1,238	1,316	1,434	1,370
London	2,537	2,583	2,529	2,563	2,748	2,950	3,080	3,011	3,315	3,286
Ottawa	1,997	2,078	2,190	2,248	2,573	2,847	2,929	2,963	3,117	3,327
Sudbury	-	-	-	-	-	-	-	285	311	508
Thunder Bay	369	401	462	444	435	506	505	513	552	565
Toronto-Bayview	-	441	504	816	1,251	1,826	2,264	2,774	2,982	3,460
Toronto, PMH	6,911	7,057	7,320	7,012	7,332	7,171	7,328	6,840	6,646	6,649
Windsor	898	813	907	858	960	1,038	1,053	1,095	1,137	1,208
TOTAL	16,305	16,864	17.446	17,702	19,305	20,315	21,895	22,269	23,223	24,222

[1] Excludes carcinoma of cervix in situ.
[2] Any case registered at more than one treatment centre in a given year is allocated to the centre where it was first registered.
[3] Data for the year 1988 were extracted from the centres in August 1989.

TABLE IX

New Cancer Cases Registered by Site of Disease and Treatment Centre, 1988[1]

SITE OF DISEASE	ICD9[2] NUMBER	TREATMENT CENTRE									TOTAL	
		Hamilton	Kingston	London	Ottawa	Sudbury	Thunder Bay	Toronto		Windsor	Number	Per Cent
								Bayview	PMH			
Lip	140	11	11	30	8		4	5	16	3	88	0.4%
Tongue	141	27	4	25	25	2	6	11	74	6	180	0.8%
Rest of mouth	142-145	39	9	49	30		6	26	122	8	289	1.3%
Pharynx and tonsil	146-149	44	12	39	57	4	4	40	134	13	347	1.6%
Esophagus	150	37	7	28	38	9	6	16	78	7	226	1.0%
Stomach	151	60	8	34	43	7	11	21	54	18	256	1.1%
Intestine, except rectum	152-153	144	63	136	197	29	36	95	214	71	985	4.4%
Rectum and anal canal	154	119	25	104	135	14	31	97	311	41	877	3.9%
Other digestive system	155-159	68	18	62	86	16	13	46	76	31	416	1.9%
Nose, middle ear and accessory sinuses	160	5	3	10	5		1	9	25	1	59	0.3%
Larynx	161	65	16	55	52	1	10	36	150	12	397	1.8%
Lung, bronchus and trachea	162	543	199	405	486	108	94	530	880	161	3,406	15.2%
Other respiratory	163-165	15	8	7	12	2	3	11	21	6	85	0.4%
Bone	170	9	3	12	9	1	3	7	15	1	60	0.3%
Malignant melanoma	172	127	19	55	75	11	7	200	181	23	698	3.1%
Other cancer of skin	173	298	223	204	196	4	27	394	373	169	1,888	8.4%
Breast	174-175	638	180	608	594	107	89	581	1,293	185	4,275	19.1%
Cervix uteri	180	68	14	41	47	4	6	88	161	14	443	2.0%
Other uterus	179-181-182	145	26	96	102	5	11	105	200	19	709	3.2%
Ovary, tubes and ligament	183	106	26	64	70	7	12	134	99	27	545	2.4%
Other female genital organs	184	18	4	8	17			16	26	3	92	0.4%
Prostate	185	177	68	184	161	21	41	178	315	40	1,185	5.3%
Testis	186	29	6	20	15	4	4	36	85	7	206	0.9%
Other male genital organs	187	1	2	2	1	1		3	10	1	21	0.1%
Bladder	188	68	26	40	99	11	13	47	154	27	485	2.2%
Kidney and other urinary	189	35	16	66	49	12	12	26	69	25	310	1.4%
Brain and nervous system	191-192	62	14	86	74	3	6	84	166	15	510	2.3%
Thyroid gland	193	10	3	12	4	4	6	4	57	1	101	0.5%
Lymphosarcoma and reticulum cell sarcoma	200	45	20	70	70	23	11	87	197	23	546	2.4%
Hodgkin's disease	201	41	9	34	26	10	7	60	126	11	324	1.4%
Other lymphomas	202	112	23	60	57	13	14	44	96	13	432	1.9%
Leukemia	204-208	89	32	84	50	25	15	42	153	29	519	2.3%
Other sites	Residual	295	46	181	194	42	40	138	409	56	1401	6.3%
TOTAL MALIGNANT		3,550	1,143	2,911	3,084	500	549	3,217	6,340	1,067	22,361	100.0
Cervix uteri (in-situ)	233.1	11	2	1	8		1	3	7	3	36	
Other sites (in-situ)	230-234	64	25	61	43	5	4	88	79	25	394	
Neoplasms of uncertain behavior	235-238	34	7	35	13	3	4	16	60	21	193	
Multiple skins (see text)	173	201	195	279	187		8	139	170	95	1,274	
Seen at more than one centre		3	6	131	35	21	1	288	71	20	576	

---

[1] Data extracted from the Centres in August 1989.

[2] ICD9 - International Classification of Diseases, Ninth Revision. World Health Organization, Geneva, 1977.

TABLE X*

New Cancer Cases Registered by Place of Residence and Treatment Centre, 1988*

COUNTY, DISTRICT OR REGIONAL MUNICIPALITY**	TREATMENT CENTRE									TOTAL
							Toronto			
	Hamilton	Kingston	London	Ottawa	Sudbury	Thunder Bay	Bayview	PMH	Windsor	
Algoma, DS	8	-	12	3	19	4	17	161	-	224
Brant	231	1	9	-	-	-	-	3	-	244
Bruce	12	-	141	-	-	-	4	10	-	167
Carleton, Ottawa RG	-	4	1	1,635	-	-	4	10	-	1,654
Cochrane, DS	10	4	2	23	10	13	10	130	-	202
Dufferin	2	-	1	-	-	-	14	44	1	62
Dundas	1	7	-	41	-	-	-	-	-	49
Durham, RG	2	-	1	2	-	-	117	365	1	488
Elgin	-	-	150	-	-	-	1	-	-	151
Essex	2	2	78	-	-	-	5	15	1,019	1,121
Frontenac	2	372	-	5	-	-	3	10	-	392
Glengarry	-	5	-	44	-	-	1	1	-	51
Grenville	-	39	-	48	-	-	-	2	-	89
Grey	5	-	155	1	-	-	12	63	-	236
Haldimand-Norfolk, RG	190	-	65	-	-	-	-	5	1	261
Haliburton	-	1	-	-	1	-	3	25	-	30
Halton, RG	386	-	5	1	-	-	26	211	-	629
Hastings	1	255	2	10	-	-	14	55	-	337
Huron	1	-	121	-	-	-	1	3	-	126
Kenora	-	2	2	-	-	36	1	1	-	42
Kent	1	-	234	1	-	-	2	5	22	265
Lambton	-	-	312	-	-	-	2	5	1	320
Lanark	-	36	-	109	-	-	-	2	-	147
Leeds	-	174	1	24	-	-	2	2	-	203
Lennox and Addington	-	83	-	-	-	-	1	2	-	86
Manitoulin, DS	-	-	2	-	14	-	1	7	-	24
Middlesex	3	1	872	2	-	-	5	7	1	891
Muskoka, RG	1	1	3	2	-	-	22	84	-	113
Niagara, RG	853	1	5	1	1	1	14	98	-	974
Nipissing, DS	5	1	2	11	17	1	14	175	-	226

TABLE X* (Continued)

New Cancer Cases Registered by Place of Residence and Treatment Centre, 1988*

COUNTY, DISTRICT OR REGIONAL MUNICIPALITY**	TREATMENT CENTRE									TOTAL
	Hamilton	Kingston	London	Ottawa	Sudbury	Thunder Bay	Toronto		Windsor	
							Bayview	PMH		
Northumberland	-	30	-	1	-	-	34	93	-	158
Oxford	8	-	204	-	-	-	1	11	-	224
Parry Sound, DS	3	-	2	1	4	1	19	85	-	115
Peel, RG	10	1	3	-	-	-	171	585	-	770
Perth	-	-	157	-	-	-	1	1	-	159
Peterborough	1	1	2	1	-	-	37	208	-	250
Prescott	1	1	-	96	-	1	-	-	-	99
Prince Edward	-	59	-	2	-	-	4	3	-	68
Rainy River, DS	2	-	1	-	-	43	-	2	-	48
Renfrew	1	2	-	250	-	-	-	7	-	260
Russell	-	-	-	55	-	-	-	-	-	55
Simcoe	3	1	4	2	1	-	179	308	-	498
Stormont	1	7	-	160	-	-	-	1	-	169
Sudbury, RG and DS	8	1	2	7	408	-	11	224	-	661
Thunder Bay, DS	5	1	2	1	2	439	3	24	1	478
Timiskaming, DS	4	-	2	9	6	1	11	77	-	110
Victoria	-	-	-	-	-	-	27	105	1	133
Waterloo, RG	121	4	280	2	-	-	19	57	1	484
Wellington	221	-	37	-	-	1	12	30	-	301
Wentworth, Hamilton RG	1,157	3	5	1	-	-	7	12	-	1,185
York/Metro Toronto RG	12	8	8	6	1	1	2,266	2,850	1	5,153
Quebec	-	7	2	461	1	-	16	16	1	504
Other Provinces	6	9	15	38	8	6	42	74	-	198
U.S.A.	-	13	6	10	3	1	13	14	7	67
Other World	3	1	3	11	4	-	32	43	1	98
Residence at diagnosis not stated	267	5	-	7	-	-	16	9	8	312
TOTAL	3,550	1,143	2,911	3,084	500	549	3,217	6,340	1,067	2,2361

*Data extracted from the Centres in August, 1989.

**DS = District, RG = Regional Municipality, others are Counties.

DIRECTORY

MEMBERS OF THE ONTARIO CANCER TREATMENT AND RESEARCH FOUNDATION AND ITS COMMITTEES

(As constituted at December 31, 1989)

THE OCTRF BOARD

Chairman:

MICHAEL A. MEIGHEN, LL.L., Q.C	Toronto

President and Chief Executive Officer:

J.W. MEAKIN, M.D., C.M., M.A., F.R.C.P.(C)	Toronto

Members:

G.M. ADAMS	Thunder Bay
K.R. CLARKE, C.A.	Ottawa
M.M. CONROY, B.Sc.N., Reg.N.	Sudbury
G.P. ELIGH, B.Comm.	Kingston
S. GELLER, B.A.	Toronto
C.A.D.G. HURTEAU, M.D., C.M., L.M.C.C., F.R.C.S.(C), F.A.C.O.G.	Ottawa
G. GENCHI	Mississauga
Rev. W.K. JAGGS, L.Td., M.A., D.Min.	Windsor
MRS. BETTE JOHNSTON, Reg.N.	Toronto
J.J. KIME, C.A.	Toronto
L.M. KUSHNIR, M.L.S., LL.B.	Toronto
W. LIVINGSTON, B.Comm.	Toronto
D.M. MacKENZIE, M.A., D.H.A.	Toronto
L. SIMINOVITCH, O.C., Ph.D., F.R.S.C., D.Sc.	Toronto
B.M. THALL, M.A.Sc., Ph.D.	Toronto
G.R. WALKER, M.D., D.A.B.S., F.A.C.S., F.R.C.S.(C)	Subury
C. WAXMAN	Hamilton
D.B.WEBBER, B.B.A., F.C.S.I.	London
J.Y.K. WONG, M.D.	Toronto

Secretary:

J.W. MEAKIN, M.D., C.M., M.A., F.R.C.P.(C)	Toronto

AUDIT AND FINANCE COMMITTEES

Chairman:

G.M. Adams	Thunder Bay

Vice-Chairman:

C. Waxman	Hamilton

Secretary:

J.W. Meakin, M.D., C.M.	Toronto

Members:

M.A. Meighen, Q.C., LL.L.	Toronto
J.J. Kime, C.A.	London
L. Kushnir, LL.B.	Toronto
W. Livingston, B.Comm.	Toronto
B.M. Thall, Ph.D.	Toronto

INVESTMENT COMMITTEE

Chairman:

D.B. Webber, B.B.A.	London

Secretary:

J.W. Meakin, M.D., C.M.	Toronto

Members:

W. Foote	Toronto
W.R. Livingston, B.Comm.	Toronto
M.A. Meighen, Q.C.	Toronto
J. Payzant, B.Comm.(Hon)	Toronto
B.M. Thall, Ph.D.	Toronto

CANCER RESEARCH ADVISORY PANEL

Chairman:

L. Siminovitch, C.C., Ph.D., D.Sc.	Toronto

Members:

W. Duncan, M.B., B.Ch.	Toronto
P.G. Harding, M.D.	London
E. Eisenhauer, M.D.	Kingston
J.E. Till, Ph.D.	Toronto
R. Roberts, M.Tech.	Hamilton
B.C. Wilson, Ph.D.	Hamilton

CHEMOTHERAPEUTIC AGENTS COMMITTEE

Chairman:

TBA

Members:

H.T. Abu-Zahra, M.B., B.Ch.	Windsor
B.J. Campling, M.D.	Kingston
H. Chan, M.B., B.S.	Toronto
R.E.T. Corringham, M.B., B.S.	Sudbury
C. Cripps, M.D.	Ottawa
R. Feld, M.D.	Toronto
M.T. Gannon, D.Sc.	Toronto
I.J. Kerr, M.D.	Toronto
W.I. Kocha, M.D.	London
P.B. McCulloch, M.D.	Hamilton
H. Rayner, M.D.	Thunder Bay

CONSULTANT PATHOLOGISTS COMMITTEE

Chairman:

M.S. Smout, M.D.	London

Members:

R. Bonin, M.D.	Sudbury
N. Escott, M.D.	Thunder Bay
G.L. Frank, M.B., Ch.B.	Hamilton
E.J. Holowaty, M.D.	Toronto
P.M. Manley, M.D.	Kingston
V.J. Montpetit, M.D.	Ottawa
H. Richmond, M.D.	Toronto
J.R. Srigley, M.D.	Toronto
V. Walley, M.D.	Ottawa
G.E. Yee, M.D.	Windsor

RECORDS AND STATISTICS COMMITTEE

Chairman:

E.A. Clarke, M.B., B.S.	Toronto

Members:

T.D.R. Briant, M.D.	Toronto
W.R. Bruce, Ph.D., M.D.	Toronto
R. Feld, M.D.	Toronto
M. Goodyear, M.B., B.S.	Hamilton
R.D.T. Jenkin, M.B., B.S.	Toronto
W.I. Kocha, M.D.	London
J.F. Kotalik, M.D.	Thunder Bay
N. Kreiger, Ph.D.	Toronto
T.F. McElligott, M.D.	Kingston
J.L. Pater, M.D.	Kingston
D. Ross, C.C.H.R.A.	London
M.S. Smout, M.D.	London
D.J. Stewart, M.D.	Ottawa
S. Yoshida, M.D.	Windsor

SENIOR MANAGEMENT COMMITTEE

Chairman:

A.R. Ganderton, C.A. (interim)	Toronto

Members:

E.A. Clarke, M.B., B.S.	Toronto
R.E.T. Corringham, M.B., B.S.	Sudbury
N.J. Devereaux, C.G.A.	Toronto
W.K. Evans, M.D.	Ottawa
A.D. Ginsburg, M.D.	Kingston
W.M. Hryniuk, M.D.	Hamilton
R.D.T. Jenkin, M.M.B., B.S.	Toronto
J.F. Kotalik, M.D.	Thunder Bay
J.C. Laidlaw, M.D.	Toronto
L. Levin, M.D.	London
L.V. MacLean, B.A.	Toronto
J.W. Meakin, M.D., C.M.	Toronto
G.C.K. Mok, M.D.	Windsor

FOUNDATION HEAD OFFICE STAFF

President and Chief Executive Officer:
J. William Meakin, M.D., C.M.

Executive Vice-President and Chief Operating Officer:
Rik Ganderton, C.A. (interim)

Head, Division of Epidemiology and Statistics and Vice-President OCTRF:
E. Aileen Clarke, M.B., B.S.

Vice-President Research and Education:
John C. Laidlaw, M.D.

Chief Financial Officer:
Nelson J. Devereaux, C.G.A.

Director Human Resources:
Loraine V. MacLean, B.A.

Manager Information Systems:
TBA

Internal Auditor:
Jerome Y. Porat, B.Comm., C.P.A.(Isr.)

Editor of Publications:
John O. Godden, M.D., C.M.

APPENDICES

APPENDIX A

BEQUESTS AND OTHER DONATIONS

The Foundation was the grateful recipient of legacies, bequests and other donations totalling $3,689,278 for the fiscal year ending March 31, 1989, which are of inestimable value to the Foundation's program.

Legacies of $1,000 or over were received during the above period from the following estates:

The late Edith Allison, Kingston for use at Kingston Centre	$ 35,085
– Mary Ashton, Thunder Bay	5,000
– Eunice H. Ballantyne, Clearwater, Florida in memory of Dr. Norman A. McCormick	U.S. 1,000
– Helena Brown, Toronto	2,000
– Ina Bugg, London for use at London Centre	9,000
– Nellie Burke, Toronto	5,000
– Mary Cowie Binnie Cattell, Toronto	1,000
– Ada Christner, Kitchener	3,571
– Robena Campbell Clark, Guelph	69,261
– Beecher Dennis, Toronto	35,519
– Eldred Durham, Toronto (Ann and Eldred Durham Trust Fund) for research	6,924
– Eva Rae Forbes, Forest for use at Thameswood Lodge, London	7,500
– Birtle Milo Francis, Exeter	48,340
– Mary Myrtle Francis, Exeter	18,341
– John Jacob Freedman, Toronto	5,000
– Delmar Forest Gahm, Toronto	5,000
– Norman Parks Garrett, Blyth	111,182
– Catherine Gibson, Toronto	1,000
– Erma Zoe Louise Goering, Hamilton for research at Hamilton Centre	6,800
– Russell J. Grundy, Toronto	5,000
– Florence Campbell Houston, Scarborough	4,000
– Arthur James Hurle, Vancouver for promotion of cancer research and treatment facilities	48,696
– Grace Jones, Simcoe	5,000

– Earl W. Keutch, Rodney for use at London Centre	2,000
– Ethel May Lamb, Leamington	2,500
– Isabel Lees, Toronto	8,400
– Elma Winnifred Lister, London for use at London Centre	2,000
– Sarah Marjorie Martin, Township of Mara, County of Simcoe	150,000
– Ida Elenora Mortensen, Oshawa	71,036
– Ethel Mutter, Toronto	6,350
– Amy E. McArthur, Toronto	1,000
– Robert Pickard McBride, Hamilton	2,016,878
– Ena Beatrice Nelson, London	2,149
– Mary Jane O'Prey, Toronto	55,000
– Margaret Ann Padmore, Ottawa in memory of her brother, William Padmore, for use at Ottawa Centre	3,000
– Irma Piwczyk, Nepean for use at Ottawa Centre	44,727
– Eva Porter, Hamilton	23,964
– John Bruce Archer Reeson, Oshawa	73,984
– Dorothea Elizabeth Prouse Richards, Hamilton	10,100
– Bertha Mabel Richter, London (Richter Endowment Fund Trust) for use at London Centre	157,100
– Rhea M. Ritchie, Vancouver	30,075
– Joan Alison Sanborn, Toronto	11,000
– Clara Bell Sanderson, Brantford (The John A. Sanderson Family Trust)	10,042
– Margaret Augusta Sidor, Fort Erie for use at Lakeview Lodge, Hamilton	2,000
– Dorothy Rose, Smeaton, Windsor for use at Windsor Centre	10,000
– Peggy Snider, Burlington	5,000
– Mary Jane Steinbeck, Toronto	5,000
– Lewis Taylor, Goderich	4,384
– Dorothy Thurston, Ottawa	21,934
– John Carlaw Walker, Toronto	25,000
– May Maude Wilkinson, Leamington	1,000

Donations of $1,000 or more were received from the following:

– Louis Aldrovandi, Woodbridge in memory of Nancy Aldrovandi for Pain Pump Program at Toronto-Bayview Centre	3,000
– Anonymous, Ottawa for research at Ottawa Centre	1,000
– Axotec International Inc., Windsor for use at Windsor Centre	1,000
– Dr. Bernard Balinsky, Willowdale for use at Toronto-Bayview Centre	1,000
– K.A. Bloxham, Scarborough for Pain Pump Program at Toronto-Bayview Centre	3,500
– Irene Boulton, Windsor for research at Windsor Centre	1,000
– Charles F. Brooks, Atikokan for use at Amethyst Lodge, Thunder Bay	1,000
– Canadian Cancer Society Ontario Division, Toronto for purchase of CADD-PCA Pump for Windsor Centre	6,700
– Sybil Catford, Trenton for use at Kingston Centre	1,141
– The Cheung Family, Thornhill for melanoma research at Toronto-Bayview Centre	2,300
– Anna R. Cundhill, Ottawa for use at Ottawa Centre	1,000
– Walter Fischer, Kitchener for use at Thameswood Lodge, London	2,500
– Foley Agricultural Society (Nevada), Parry Sound for use at Lakeview Lodge, Hamilton	2,000
– Forest City Youth Slow-Pitch Association, London for use in oncological education at London Centre	3,010
– Mary Fox, Fox & Associates, Windsor for diagnostic computer for Windsor Centre	5,000
– Garrett Canada Employees Charity Fund, Toronto for Pain Pump Program at Toronto-Bayview Centre	3,500

– Karen and Subhash Ghelani, Richmond Hill for research in pediatric radiotherapy at Toronto-Bayview Centre	2,501
– Gore Mutual Insurance Company, Cambridge in memory of George H. Lochead, Q.C.	1,000
– John W. Grand, Toronto in memory of J.R. Grand, for research	2,000
– Simone Gravelle, Gloucester for use at Ottawa Centre, General Division	1,000
– Romeo Hachey, Windsor for use at Windsor Centre	4,000
– Mary Hall, Amherstburg for treatment planning computer at Windsor Centre	1,000
– Jean Hogan, Kingston for use at Kingston Centre	1,000
– Hospice of Windsor Inc., Windsor for purchase of CADD-PCA Pump and toys at Windsor Centre	10,000
– Mr. and Mrs. Edward Huber, Waterloo for use at Thameswood Lodge, London	1,000
– L. King Hughes, Don Mills for research at Toronto-Bayview Centre	1,000
– Marr A. Huson, Windsor for use at Windsor Centre	1,000
– I.C.I. Pharma, Mississauga for research	1,800
– Linda Innes, Sudbury for use at Northeastern Ontario Oncology Program in Sudbury	1,000
– Constance N. James, Balderson for use at Maurice Grimes Lodge, Ottawa	1,000
– Knights of Columbus, Council 2844, McGregor for use at Windsor Centre	1,000
– Knockers Club of Canada, Nepean for hyperthermia equipment at Ottawa Centre	1,000
– Marietta Kosovsky, New York, N.Y. in memory of Dr. Jonah Kosovsky for research at Northeastern Ontario Oncology Program in Sudbury	2,403
– Theresa Kulker, Design Built, Kitchener for use at Thameswood Lodge, London	1,000

– Bruce Long, Toronto in memory of his wife, Mary, for research	1,000
– Mr. & Mrs. T. Main, Thunder Bay for purchase of chemotherapy chair for Thunder Bay Centre	1,200
– Metropolitan General Hospital, Windsor for use at Windsor Centre	1,000
– John H. Moore, London for new research at London Centre	5,000
– Donald Morphy, London in memory of Carole Ann Miles for palliative care at Windsor Centre	2,000
– Joyce M. Nichols, Windsor for use at Windsor Centre	1,000
– Mary Novakovich, Sudbury for use at Northeastern Ontario Oncology Program in Sudbury	1,000
– Olympia & York Developments Ltd., Toronto for use at Ottawa Centre	2,000
– John O'Neill, Willowdale for research at Toronto-Bayview Centre	1,000
– Mario and Antonia Paolucci Charitable Foundation, Willowdale	1,000
– Quality Door Hardware Ltd., Thunder Bay for purchase of chemotherapy chair for Thunder Bay Centre	1,200
– Employees of Royal Bank of Canada Main Branch, Toronto	3,064
– Royal Canadian Legion Ladies Auxiliary, Branch 39, Espanola for building fund, Northeastern Ontario Oncology Program in Sudbury	5,000
– Royal Canadian Legion, Northern Ontario Memorial, Branch 415, Port Loring, for use at Northeastern Ontario Oncology Program in Sudbury	1,000
– Lola M. Shaw, Manotick for purchase of research equipment at Ottawa Centre	2,000
– Sara Lee Kitchens Canada, Brampton in memory of Peter Samonig, for research at Toronto-Bayview Centre	1,000
– L. Townson, Thunder Bay for research at London Centre	1,500

– Tupperware New Zealand, Auckland in memory of Gwen Farthing	1,000
– Arthur and Melba Weaver, Sutton West in memory of Dollie Kirkpatrick	1,000
– Peggy Williamson, Athens in memory of Greg Williamson for use at Kingston Centre	1,000
– Sam Wilson, Brighton for use at Kingston Centre	3,000

The Foundation is grateful to these donors and to the many others not listed above and it reveres the memory of those who, when making their wills, extended beyond their lifetime the fight against cancer. These welcome additions to our research and other funds ensure that the Foundation's extensive cancer control programs can proceed at a time of financial constraints and inflated costs.

APPENDIX B

LIST OF ARTICLES PUBLISHED IN 1988 BY CAREER SCIENTISTS, RESEARCH ASSOCIATES,GRANTEES, MEMBERS OF THE OCTRF STAFFS AT THE REGIONAL CANCER CENTRES AND HEAD OFFICE AND THE OCI/PMH

HAMILTON

OCTRF Hamilton Regional Cancer Centre:

BABICH JW, KEELING F, FLOWER MA, REPETTO L, WHITTON A, FIELDING S, FULLBROOK A, OTT RJ, McCREEADY VR: Initial experience with Tc-99m-HMPAO in the study of brain tumours. *Eur J Nucl Med* 1988; **14:** 39.

BROWMAN G, LEVINE MN, HODSON DI, RUSSELL R, McALPINE L, GOODYEAR M, SATHYA J, RIDER W: A new quality of life index for head and neck cancer patients receiving radical radiotherapy. *Proc Am Soc Clin Oncol* 1988; **7:** 157. (Abstract C-597)

BROWMAN GP, LEVINE MN, GOODYEAR MD, RUSSELL R, ARCHIBALD SD, JACKSON S, YOUNG JEM, BASRUR V, JOHANSON C: Methotrexate/5-fluorouracil scheduling influences normal tissue toxicity but not anti-tumor effects in patients with squamous cell and head and neck cancer: Results from a randomized trial. *J Clin Oncol* 1988; **6:** 963.

COY P, HODSON DI, PAYNE D, EVANS WK, FELD R, McDONALD AS, OSOBA D, PATER J: Effect of dose of thoracic radiotherapy on recurrence in patients with limited small cell lung cancer: Initial results of a Canadian multicentre randomized trial. *Int J Radiat Oncol Biol Phys* 1988; **14:** 219.

FLOCK ST, WILSON BC, PATTERSON MS: Hybrid Monte Carlo-diffusion theory modelling of light distributions in tissue. *Proc SPIE* 1988; **908:** 20.

HIRSH J, LEVINE MN: Confusion over the therapeutic range for monitoring oral anticoagulant therapy in North America. *Thromb Haemost* 1988; **59:** 129.

HRYNIUK WM: More is better. *J Clin Oncol* 1988; **6:** 1365. (Editorial)

JAMER RD, WILLIAMS P, JONES A, NELLIS P, FARROW N, LUKKA HR, PYE DW: Determination of human skin pain threshold using 27 MHz radio frequency heating. *Br J Radiol* 1988; **61:** 344.

JEEVES WP, WILSON BC, SPIEGL P, SMITH P: DHE uptake and PDT response in an in vitro tumor model. *In:* Moreno G, Pottier RH, Truscott TG, eds. Photosensitization: Molecular, Cellular and Medical Aspects. New York: Springer-Verlag Publishers, 1988: 469.

KWOK CS, COLE S, LIAO SK: Uptake kinetics of monoclonal antibodies by human malignant melanoma multicell spheroids. *Cancer Res* 1988; **48:** 1856.

LEVINE MN, GENT M, HIRSCH J, ARNOLD A, GOODYEAR MD, HRYNIUK W, DEPAUW S: The thrombogenic effect of anti-cancer drug therapy in women with Stage II breast cancer. *N Engl J Med* 1988; **318:** 404.

LEVINE MN, GUYATT G, GENT M, DEPAUW S, GOODYEAR M, KRYNIUK WM, ARNOLD A, FINDLAY B, SKILLINGS JR, BRAMWELL VH, LEVIN L, BUSH H, ABU-ZAHRA J, KOTALIK J: Quality of life in Stage II breast cancer: an instrument for clinical trials. *J Clin Oncol* 1988; **6:** 1798.

LEVINE MN, HIRSH J: An overview of clinical trials of low molecular weight heparin fractions. *Acta Chir Scand Suppl* 1988; **543:** 73.

LEVINE MN, HIRSH J: Clinical use of low molecular weight heparins and heparinoids. *Semin Thromb Hemost* 1988; **14:** 116.

MARCURHAMER S, MacLEAN GD, McEWAN AJ, LONGACKER BM, SYKER TR, LUKKA HR, NOUJAIM AA: Immuno scintigraphy of lung adenocarcinoma using a novel monoclonal antibody. *Am Rev Respir Dis* 1988; **137:** 457. (Abstract)

MBIDDE EK, SELBY PJ, PERREN TJ, DEARNALEY DP, WHITTON A, ASHLEY S, WORKMAN P, BLOOM HJG, McELWAIN TJ: High dose BCNU chemotherapy with autologous bone marrow transplantation and full dose radiotherapy for Grade IV astrocytoma. *Br J Cancer* 1988; **58:** 779.

McFADDEN R, KWOK CS: Mathematical model of simultaneous diffusion and binding of anti-tumor antibodies in multicell tumor spheroids. *Cancer Res* 1988; **48:** 4032.

NEVILLE AJ, SAUDER DN: Whole body hyperthermia (40-42^{o}C) induces interleukin-1 in vivo. *Lymphokine Res* 1988; **7:** 201.

PATTERSON MS, WILSON BC, GRAFF R: Applications of the change in tissue optical properties caused by the presence of photosensitizers. *In:* Moreno G, Pottier RH, Truscott TG, eds. Photosensitization: Molecular, Cellular and Medical Aspects. New York: Springer-Verlag Publishers, 1988: 121.

PORTER AT, LUKKA HR, McEWAN AJ, McLEAN G: Lymph node evaluation using computed tomography and immunoscintigraphy in prostate cancer. *Clin Radiol* 1988; **39:** 352.

ROBINS HI, KALIN NH, SHELTON SE, MARTIN PA, SCHECTERLE LM, BARKSDALE CM, NEVILLE AJ, MARSHALL J: Rise in plasma beta-endorphin, ACTH, and cortisol in cancer patients undergoing whole body hyperthermia. *Horm Metab Res* 1988; **19:** 441.

ROBINS HI, LONGO WL, LAGONI RK, NEVILLE AJ, HUGANDER A, SCHMITT CL, RIGGS C: A phase I trial of lonidamine with whole body hyperthermia in advanced cancer. *Cancer Res* 1988; **48:** 6587. lung cancer confined to the thorax.

ROBINS HI, LONGO WL, STEEVES RA, LOGONI RK, HUGANDER A, NEVILLE AJ, O'KEEFE S, GIESE W, SCHMITT CL: A pilot study of whole body hyperthermia and local irradiation for advanced non-small cell lung cancer confined to the thorax. *Int J Radiat Oncol Biol Phys* 1988; **15:** 427.

RUSTHOVEN JJ: The challenge of curing cancer: Increasingly complex patient management planning. *Humane Med* 1988; **4:** 12.

RUSTHOVEN JJ, AHLGREN P, ELHAKIM T, PINFOLD P, REID J, STEWART L, FELD R: Varicella-zoster infection in adult cancer patients: A population study. *Arch Intern Med* 1988; **148:** 1561.

RUSTHOVEN JJ, AHLGREN P, ELHAKIM T, PINFOLD P, STEWART L, FELD R: Risk factors for varicella-zoster disseminated infection among adult cancer patients with localized zoster. *Cancer* 1988; **62:** 1641.

RUSTHOVEN J, WIERZBICKI R, VERMA S: A Phase II study of trimetrexate in metastatic soft tissue sarcoma. Proc Am Soc Clin Oncol 1988; **7:** A1066. (Abstract)

SHUMAK SL, SCRIGLEY J, RUSTHOVEN JJ, COWAN DH: Hodgkin's disease complicating untreated non-Hodgkin's lymphoma. *Can Med Assoc J* 1988; **139:** 1157.

SINGH G, SHAUGHNESSY SG: Functional impairment induced by lipophilic cationic compounds on mitochondria. *Can J Phys Pharmacol* 1988; **66:** 243.

SINGH G, KOROPATNICK J: Differential toxicity of cis and trans isomers of dichlorodiammineplatinum. *J Biochem Toxicol* 1988; **3:** 223.

TANSER CL: Potential phototoxicity in the photosensitive patient. *In:* Moreno G, Pottier RH, Truscott TG, eds. Photosensitization: Molecular, Cellular and Medical Aspects. New York: Springer-Verlag Publishers, 1988: 499.

WEITZ JI, CRUICKSHANK MK, THONG B, LESLIE B, LEVINE MN, GINSBERG J, ECKHARDT T: Human tissue-type plasminogen activator releases fibrinopeptides A and B from fibrinogen. *J Clin Invest* 1988; **82:** 1700.

WERNER BL, KWOK CS, DAS IJ: Dose distributions in regions containing beta sources. *Med Phys* 1988; **15:** 358.

WILSON BC, FIRNAU G, JEEVES WP, BROWN KL, BURNS DM, HEYNEN M: Chromatographic analysis and tissue distribution of radiocopper labelled hematoporphyrin derivatives. *Lasers Med Sci* 1988; **3:** 71.

WILSON BC, FLOCK ST, PATTERSON MS: The optical properties of tissues at 633 nanometers as related to light dosimetry in photodynamic therapy. *In:* Moreno G, Pottier RH, Truscott TG, eds. Photosensitization: Molecular, Cellular and Medical Aspects. New York: Springer-Verlag Publishers, 1988: 117.

WILSON BC, PATTERSON MS, FLOCK ST, MOULTON JD: The optical obsorption and scattering properties of tissues in the visible and near-infrared wavelength range. *In:* Douglas RH, Moan J, Dall'Acqua F, eds. Light in Biology and Medicine: New York: Plenum Publishers, 1988: 45.

WONG ZM, TEARE FW, BOWEN BM, LIAO SK, KWOK CS, BOXEN I: Comparison of the iodogen and the microelectrochemical techniques for the radioiodination of monoclonal antibody 140.240. *Nucl Med Biol* 1988; **15:** 505.

WYMAN DR, PATTERSON MS: A discrete method for anisotropic angular sampling in Monte Carlo simulations. *J Comp Phys* 1988; **76:** 414.

KINGSTON

OCTRF Kingston Regional Cancer Centre:

ALVAREZ E, ELLIOTT BE, HOUGHTON AN, KERBEL RS: Heritable high frequency modulation of antigen expression in neoplastic cells exposed to 5-Aza-2-deoxycytidine or hydroxyurea: Analysis and implications. *Cancer Res* 1988; **48:** 2440.

CAMPLING BG, PYM J, GALBRAITH PR, COLE SPC: Use of the MTT assay for rapid determination of chemosensitivity of human leukemic blast cells. *Leukemia Res* 1988; **12:** 823.

COCHRANE A, DEELEY RG: Detection and characterization of degradative intermediates of avian Apo very low density lipoprotein II mRNA present in estrogen treated birds and following destabilization by hormone-withdrawal. *J Biol Chem* 1988; **264:** 6495.

COCHRANE AW, DEELEY RG: Estrogen-dependent activation of the avian very low density apolipoprotein II and vitellogenin genes: Transient alterations in mRNA polyadenylation and stability early during induction. *J Mol Biol* 1988; **203:** 555.

COLE SPC, DOWNES HF, SLOVAK ML: Effect of calcium antagonists on multidrug resistant tumor cell lines which lack P-glycoprotein. *Proc Am Assoc Cancer Res* 1988; **29:** 1235. (Abstract)

DILLON J, KENNEDY JC, POTTIER RH, ROBERTS JE: In vitro and in vivo protection against phototoxic side effects of photodynamic therapy by radioprotective agents WR-2721 and WR-77913. *Photochem Photobiol* 1988; **48:** 235.

EISENHAUER EA, EVANS WK, MURRAY N, KOCHA W, WIERZBICKI R, WILSON K: A phase II study of VP-16 and cisplatin in patients with unresectable malignant mesothelioma: An NCIC Clinical Trials Group study. *Invest New Drugs* 1988; **6:** 327.

EISENHAUER EA, ZEE BC, PATER JL, WALSH WR: Trimetrexate: Predictors of severe or life-threatening toxicity. *J Natl Cancer Inst* 1988; **80:** 1318.

ELLIOTT BE, MAXWELL L, ARNOLD M, WEI WZ, MILLER FR: Expression of epithelial-like markers and Class I major histocompatibility antigens by a murine carcinoma growing in the mammary gland and in metastasis: Orthotopic site effects. *Cancer Res* 1988; **48:** 7237.

ELLIOTT CR, PATER JL: The effect of different measures of outcome on the results of studies of empiric antibiotic therapy in febrile neutropenic patients. *Clin Invest Med* 1988; **11:** 327.

HACHE RJG, DEELEY RG: Oraganization, sequence and nuclease hypersensitivity of repetitive elements flanking the chicken apoVLDL gene: Extended homology with elements flanking the chicken vitellogenin gene. *Nucl Acids Res* 1988; **16:** 97.

JAACKIMAIMEN L, GOODWIN PJ, PATER JL, WARDE P, RAPP E: Combination chemotherapy for advanced non-small lung cancer (NSCLC): Effective but at what cost? *Lung Cancer* 1988; **4(Suppl):** A181.

JOHNSON JF, EISENHAUER EA, CORBETT WEN, SCOTT JG, ZAENTZ SD: The efficacy of 2'-deoxycoformycin in hairy cell leukemia: A study of the National Cancer Institute of Canada Clinical Trials Group. *J Natl Cancer Inst* 1988; **80:** 765.

KENNEDY JC: Photochemotherapy – clinical aspects. *In:* Moreno G, Pottier RH, Truscott, eds. Photosensitization: Molecular, Cellular and Medical Aspects. New York: Springer-Verlag Publishers, 1988: 453.

PATERSON PE, WEAGLE G, POTTIER R, KENNEDY J: In vivo fluorescence from mouse skin: Spectral evidence for the presence of chlorophyll derivatives. *In:* Moreno G, Pottier RH, Truscott TG, eds. Photosensitization: Molecular, Cellular and Medical Aspects. New York: Springer-Verlag Publishers, 1988: 465.

PATERSON P, WEAGLE G, POTTIER R, KENNEDY J: Naturally occurring chlorophyll degradation products detected in mouse skin. *Photochem Photobiol* 1988; **47:** 55S. (Abstract WAM-B9)

POTTIER R, LACHAINE A, PIERRE M, KENNEDY JC: A new electronic absorbance band in concentrated aqueous solutions of hematoporphyrin IX detected by photoacoustic spectroscopy. *Photochem Photobiol* 1988; **47:** 669.

POTTIER RH, KENNEDY JC, CHOW YFA, CHEUNG F: The pKa values of hematoporphyrin IX as determined by absorbance and fluorescence spectroscopy. *Can J Spectr* 1988; **33:** 57.

POTTIER RH, WEAGLE G, PATERSON PE, KENNEDY J: The nature of the chromophore responsible for naturally occurring fluorescence in mouse skin. *J Photochem Photobiol* (B: Biology) 1988; **2:** 313.

QUIRT A, EISENHAUER E, KNOWLING M, WARR D, BRAMWELL V, RUSTHOVEN J, WIERZBICKI R, VERMA S: A Phase II study of trimetrexate in metastatic soft tissue sarcoma: A co-operative study of the Canadian Sarcoma Group and the National Cancer Institute of Canada. *Proc Am Soc Clin Oncol* 1988; **7:** 275. (Abstract 1060)

RAPP E, PATER JL, WILLAN A, CORMIER Y, MURRAY N, EVANS WK, HODSON I, CLARK DA, FELD R, ARNOLD AM, AYOUB JI, WILSON KS, LATREILLE J, WIERZBICKI RF, HILL DP: Chemotherapy can prolong survival in patients with advanced non-small-cell lung cancer – Report of a Canadian multicenter randomized trial. *J Clin Oncol* 1988:**6:** 633.

RAPP E, PATER JL, WILLAN A, CORMIER Y, MURRAY N, EVANS WK, HODSON DI: Combination chemotherapy confers a modest survival advantage in patients with advanced non-small cell lung cancer: Report of a Canadian multicentre trial. *Semin Oncol* 1988; **15:** 42.

TAM S-P, STRUGNELL S, DEELEY RG, JONES G: 25-hydroxylation of Vitamin D_3 in the human hepatoma cell lines Hep G2 and Hep 3B. *J Lipid Res* 1988; **29:** 1637.

TRENT JM, MELTZER PS, SLOVAK ML, HILL AB, DALTON WS, BECK WT, COLE SPC: Cytogenetic and molecular biologic alterations associated with anthracycline resistance. *In:* Woolley PV, Tew KD, eds. Mechanisms of Drug Resistance in Neoplastic Cells. Vol. 9. New York: Academic Press, 1988: 259.

LONDON

OCTRF London Regional Cancer Centre:

ANTOLAK J, MAH E, BATTISTA JJ, SCRIMGER JW: Acquisition and display of radiation dose distibutions using microcomputer technology. *Med Phys* 1988; **15:** 924.

BARDIN CW, GUNSALUS GL, MUSTO NA, CHENG CY, REVENTOS J, SMITH CL, UNDERHILL DA, HAMMOND GL: Corticosteroid binding globulin, testosterone-estradiol binding globulin and androgen binding protein belong to protein families distinct from steroid receptors. *J Steroid Biochem* 1988; **30:** 131.

BRAMWELL VHC: Intra-arterial chemotherapy of soft tissue sarcomas. *Semin Surg Oncol* 1988; **4:** 66.

BRAMWELL VHC: The role of chemotherapy in multi-modality therapy. *Can J Surg* 1988; **31:** 390.

BRAMWELL VHC, BLACKLEDGE G, BUESA J et al: A review of the clinical trials activity of the Soft Tissue and Bone Sarcoma Group (STBSG) of the European Organization for Research and Treatment of Cancer (EORTC). *Semin Surg Oncol* 1988; **4:** 45.

BRAMWELL VHC, EISENHAUER E: A pilot study of Adriamycin, dacarbazine and ifosfamide in advanced adult soft tissue sarcomas: A prelimary report from the Canadian Sarcoma Group of the National Cancer Institute of Canada Clinical Trials Group. *In:* Ryan JR, Baker LH, eds. Recent Concepts in Sarcoma Treatment. Dordrecht, The Netherlands: Kluwer Academic Publishers, 1988: 169.

BRAMWELL VHC, ROCK M, WORTH A, SHIBATA H, O'SULLIVAN B: Management of soft tissue sarcomas. *Ann R Coll Phys Surg Can* 1988; **21:** 331.

CAIRNCROSS JG, MacDONALD DR: Succesful chemotherapy for malignant oligodendroglioma. *Ann Neurol* 1988; **23:** 360.

CAIRNCROSS JG, MacDONALD DR, PEXMAN JHW, IVES FJ: Steroid induced CT scan changes in patients with recurrent malignant glioma. *Neurology* 1988; **38:** 724.

CHAMBERS AF, HARRIS JF, GRUNDY JS: Rates of generation of methotrexate-resistant variants in cells that are temperature-sensitive for malignant transformation. *Somat Cell Mol Genet* 1988; **14:** 253.

CHAMBERS AF, HARRIS JF, GRUNDY JS: Rates of generation of methotrexate-resistant variants in cells that are sensitive for malignant transformation. *Genome* 1988; **30(Suppl 1):** 196. (Abstract)

CHAMBERS AF, TUCK AB: Oncogene transofrmation and the metastatic phenotype. *Anticancer Res* 1988; **8:** 861.

CHAMBERS AF, WILSON S: Use of neoR B16F1 murine melanoma cells to assess clonality of experimental metastases in the immune-deficient chick embryo. *Clin Exp Metastasis* 1988; **6:** 171.

CRAIG AM, NEMIR M, MUKHERJEE BB, CHAMBERS AF, DENHARDT DT: Identification of the major phosphoprotein secreted by rat and mouse fibro-blasts as 2ar/osteopontin: Altered expression in *ras*-transformed cells. *Biochem Biophys Res Commun* 1988; **157:** 166.

HARRIS JF, BEST MW: Dynamic heterogeneity: Metastatic variants to liver are generated spontaneously in mouse embryonal carcinoma cells. *Clin Exp Metastasis* 1988; **6:** 451.

HARRIS JF, KOROPATNICK J, PEARSON J: Extensive loss of antibody production in heteromyeloma hybridoma cells. *Genome* 1988; **30(Suppl 1):** 433.

HILL SA, WILSON S, CHAMBERS AF: Clonal heterogeneity, experimental metastatic ability and p21 expression of H-*ras*-transformed NIH 3T3 cells. *J Natl Cancer Inst* 1988; **80:** 484.

KOROPATNICK J: Amplification of metallothionein-I genes in mouse liver cells in situ. *Proc Soc Exp Biol Med* 1988; **188:** 287.

KOROPATNICK J, CHERIAN MG: Exposure to different forms of cadmium in mice: Differences in metallothionein and alphafetoprotein mRNA induction in liver and kidney. *J Biochem Toxicol* 1988; **3:** 159.

KOROPATNICK J, PEARSON J, HARRIS J: Extensive loss of human DNA accompanies loss of antibody production in heteromyeloma hybridoma cells. *Mol Biol Med* 1988; **5:** 69.

MacDONALD DR, CAIRNCROSS JG, GILBERT JJ: Non-enhancing malignant gliomas. *Neurology* 1988; **38(Suppl 1):** 211.

MACKIE TR, BIELAJEW AF, ROGERS DWO, BATTISTA JJ: Generation of photon energy deposition kernels using the EGS Monte Carlo code. *Phys Med Biol* 1988; **33:** 1.

METCALFE PE, BATTISTA JJ: Accuracy of inhomogeneity corrections in lung irradiated with high energy x-rays. *Australas Phys Eng Sci Med* 1988: **11:** 67.

METCALFE PE, BECKHAM WA, LONG BH, BATTISTA JJ: The effect of patient density variation in radiotherapy dose calculations. *Australas Phys Eng Sci Med* 1988; **11:** 107.

NIEMI S, MAENTAUSTA O, BOLTON NJ, HAMMOND GL: A time-resolved immunofluorometric assay (tr-IFMA) for human sex hormone binding globulin (SHBG). *Clin Chem* 1988; **34:** 63.

PORTER AT, OSTROWSKI MJ: Treatment of malignant carcinoid tumour with cis-platinum. *Eur J Surg Oncol* 1988; **14:** 703.

PORTER AT, PEDERSEN JE, POCHA JS: Brachytherapy in locally advanced prostate cancer. *In:* Mould R, ed. Brachytherapy. Rotterdam: Martinus Nijhoff Publishers, 1988.

RAO AV, GOETTLER DM, BIRD RP: The effects of a "low-risk" diet on tumor incidence in chemically-induced colon cancer in rats. *Nutr Cancer* 1988; **11:** 11.

REVENTOS J, HAMMOND GL, CROZAT AS, BROOKS DE, GUNSALUS GL, BARDIN CW, MUSTO NA: Hormonal regulations of rat androgen-binding protein (ABP) messenger ribonucleic acid and homology of human testosterone-estradiol-binding globulin and ABP complementary deoxyribonucleic acids. *Mol Endocrinol* 1988; **2:** 125.

TEMPLE WJ, BRAMWELL VHC, EISENHAUER E, JENKIN RDT, LARGER F, WORTH AJ: Guidelines for the surgical management of soft tissue sarcoma: Report of the Canadian Sarcoma Group. *Can J Surg* 1988; **31:** 410.

TUCK AB, CHAMBERS AF, WILSON SM: Effect of the v-myc oncogene on progression of an L-cell line from tumorigeneic to metastatic ability. *Genome* 1988; **30(Suppl 1):** 198.

VAN UNNIK JAM, COINDRE JM, CONTESSA G, ALBUS LUTTER CHE, SCHIODT T, GARCIA-MIRALLES T, SYLVESTER R, THOMAS D, BRAMWELL VHC: Grading of soft tissue sarcomas: Experience of the EORTC Soft Tissue and Bone Sarcoma Group. *In:* Ryan JR, Baker LH, eds. Recent Concepts in Sarcoma Treatment. Dordrecht, The Netherlands: Kluwer Academic Publishers, 1988: 7.

WALKER RW, CAIRNCROSS JG, POSNER JB: Cerebral herniation in patients receiving cisplatin. *Neurooncol* 1988; **6:** 61.

WINGER MJ, MacDONALD DR, SCHOLD SC, CAIRNCROSS JG: Malignant glioma at a regional cancer centre: Implications for the interpretation of clinical trials. *Neurology* 1988; **38(Suppl 1):** 213.

OTTAWA

OCTRF Ottawa Regional Cancer Centre:

BIELAJEW AF, ROGERS DWO, CYGLER J, BATTISTA JJ: Comparison of electron pencil beam and Monte Carlo calculational methods. *In:* Bruinvis IAD, Van der Giessen PH, Van Kleffen HJ, Wittkamper FW, eds. The Use of Computers in Radiation Therapy. New York: North-Holland, 1987: 65.

BIRNBOIM HC: A superoxide anion-induced DNA strand break metabolic pathway in human leukocytes: Effects of vanadate. *Biochem Cell Biol* 1988, **66:** 374.

BIRNBOIM HC: Rapid extraction of high molecular weight RNA from cultured cells for Northern analysis. *Nucleic Acids Res* 1988; **16:** 1487.

BIRNBOIM HC: Superoxide anion may trigger DNA strand breaks in human granulocytes by acting as a membrane target. *Ann NY Acad Sci* 1988; **551:** 83.

BIRNBOIM HC: Use of fluorometric analysis of DNA unwinding (FADU) assay to detect DNA stand breaks in the liver of CD-1 mice exposed to carcinogens and a repair inhibitor. *In:* Ashby J, de Serres FJ, Shelby MD et al, eds. IPCS In-vivo Assay: Evaluation of Short-Term Tests for Carcinogens. Cambridge: Cambridge University Press, 1988: 427.

BIRNBOIM HC: Superoxide anion-induced DNA strand breaks in human neutrophils: Requirement for intracellular calcium and magnesium. *Proc Am Assoc Cancer Res* 1988; **29:** 169. (Abstract 674)

CATTON G, COY P, McGOWAN DG, DANJOUX C, FROUD P, STAAREVELD A, CUMMINGS B, RUBARTH HM, LEGOWSKI B, STARLING G: Seminar: Manpower and workload measurement in radiation oncology. *Ann R Coll Physicians Surg Can* 1988; **21:** 243.

CRIPPS C, DANJOUX C, ODELL P, EAPEN L, ESCHE BA, de la BASTIDE Y, BARRON P: Phase II study of lonidamine and radiotherapy for advanced squamous cell cancers of head and neck. *Clin Invest Med* 1988; **11:** C97.

CROOK J, MAZERON JJ, MARINELLO G et al: Combined external irradiation and interstitial implantation for T1 and T2 epidermoid carcinomas of base of tongue: The Creteil experience. *Int J Radiat Oncol Biol Phys* 1988; **15:** 105.

CYGLER J, COPELAND F: Role of CT scanning in radiation therapy with electron beam. *Med Dosimetry* 1988; **13:** 69.

CYGLER J, ROSS J: Electron dose distributions in an anthropomorphic phantom: Vertification of Theraplan treatment planning algorithm. *Med Dosimetry* 1988; **13:** 155.

CYGLER J, ROSS J: Comparison of Theraplan electron dose calculations with measurements in an anthropomorphic phantom. *Clin Invest Med* 1988; **11:** C101.

CYGLER J, ROSS J: Comparison of Theraplan electron dose calculations with measurements in an anthropomorphic phantom. *Phys Med Biol* 1988; **33:** 138.

CYGLER J, STRADOWSKI C, KROH J: Pulse radiolysis studies of n-propanol-2-methytetrahydrofurane glasses at 6-115K. *Bull Pol Acad Sci Chem* 1988; **36:** 7.

EAPEN L: Concurrent intra-arterial cisplatinum and radiation in locally advanced bladder cancer. *Int J Radiat Oncol Biol Phys* 1988; **115(Suppl 1):** 211.

EAPEN LJ, GERIG LH, CATTON GE, DANJOUX CE, GIRARD A: Impact of local radiation in the management of salivary gland carcinoma. *J Head Neck Surg* 1988; **11:** 239.

EAPEN L, STEWART DJ, DANJOUX C, GENEST P, FUTTER N, MOORS, IRVINE A, CROOK J, AITKEN S: Concurrent intraarterial cisplatin and radiation in locally advanced bladdr cancer. *Proc Am Soc Clin Oncol* 1988; **7:** 117. (Abstract)

EAPEN L, VACHET M, CATTON G, DANJOUX C, McDERMOT R, NAIR B, GIRARD A, GENEST P, STEWART D, GERIG L: Brain metastases with an unknown primary: A clinical perspective. *J Neurooncol* 1988; **6:** 31.

EAPEN LJ, VACHET M, CATTON C, DANJOUX McDERMOT R, NAIR B, GIRARD A, GENEST P, STEWART D, GERIG L: Brain metastases with an unknown primary: A clinical perspective. *J Clin Oncol* 1988; **6:** 31.

ESCHE BA, CROOK J: Interstitial implantation is essential. *Int J Radiat Oncol Biol Phys* 1988; **14:** 598.

ESCHE BA, HAIE CM, GERBAULET AP, ESCHWEGE F, RICHARD JM, CHASSAGNE D: Interstitial and external radiotherapy in carcinoma of the soft palate and uvula. *Int J Radiat Oncol Biol Phys* 1988; **15:** 619

ESCHE BA, HAIE CM, GERBAULET AP, ESCHWEGE F, RICHARD JM, CHASSAGNE D: Brachytherapy for carcinoma of the soft palate. *Clin Invest Med* 1988; **11:** C101.

EVANS WK: Nystatin lozenges: Useful treatment for oral candidiasis in cancer patients. *Int Med Digest* 1988; **4:** 21.

EVANS WK, EISENHAUER E, HUGHES P, MAROUN JA, AYOUB J, SHEPHERD FA, FELD R: VP-16 and carboplatin in previously untreated patients with extensive small cell lung cancer: A study of the National Cancer Institute of Canada Clinical Trials Group. *Br J Cancer* 1988; **58:** 464.

EVANS WK, EISENHAUER E, HUGHES P, MAROUN JA, AYOUB J, SHEPHERD FA, FELD R: VP-16 and carboplatin for previously untreated extensive lung cancer. *Lung Cancer* 1988; **4(Suppl):** A104. (Abstract 6.1.17)

EVANS WK, MURRAY N, WIERZBICKI R, SHEPHERD FA, WILSON K, SEIDENFELD A, WILSON J: Lonidamine in combination with VP-16 and cisplatin for extensive small cell lung cancer. *Lung Cancer* 1988; **4(Suppl):** A112. (Abstract 6.1.52)

EVANS WK, RAPP E, PATER JL, WILLAN A, CORMIER Y, MURRAY N, HODSON DI, CLARK DA, FELD R, ARNOLD AM, AYOUB JI, WILSON KS, LATRIELLE J, WIERZBICKI FR, HILL DP: Combination chemotherapy confers modest survival advantage in patients with advanced non-small cell lung cancer: Report of a Canadian multicentre randomized trial. *Sem Oncol* 1988; **15(Suppl 7):** 42.

EVANS WK, WIERZBICKI R, SHEPHERD FA, RUSTHOVEN J: Phase II study of 5-FU and folinic acid in metastatic adenocarcinoma of the lung. *Lung Cancer* 1988; **4(Suppl):** A126. (Abstract 6.2.36)

FEELEY MM, RAAPHORST GP, DANJOUX CE, MAROUN J, FISCHER B, MARTIN L: The response of human cells and rodent cells to lonidamine, radiation and hyperthermia. *Clin Invest Med* 1988; **11:** C96.

GERBAULET A, ESCHE BA, HAIE CM, CASTAIGNE D, FLAMANT F, CHASSAGNE D: Conservative treatment for lower gynecological tract malignancies in children and adolescents. *Int J Radiat Oncol Biol Phys* 1988; **15(Suppl 1):** 159.

GERIG LH, DANJOUX CE, HAUDEROWICZ Z, RAAPHORTS GP: A computerized thermocouple base clinical thermometry system. *Endocurietherapy* 1988; **4:** 31.

GERIG LH, RAAPHORST GP, GINSBURG A, DANJOUX CE: Measurement of blood flow by thermal washout during microwave hyperthermia. *In:* Sugahara T, Saito M, eds. London: Francis Taylor, 1988: 674.

GREEN RM, STEWART DJ, HUGENHOLTZ H, RICHARD MT, THIBAULT M, MONTPETIT V: Human central nervous system and plasma pharmacology of mitoxantrone. *J Neurooncol* 1988; **6:** 75.

GRIMARD L, EAPEN L, McDERMOT R, NAIR R: Does parasternal irradiation reduce thoracic vertebral metastases in breast cancer? *Radiology* 1988; **161:** 153.

GRIMARD L, EAPEN L, McDERMOT R, GENEST P, NAIR R: Does parasternal irradiation reduce thoracic vertebral metastases in breast cancer? *Int J Radiat Oncol Biol Phys* 1988; **14:** 565.

GRIMARD L, GENEST P, GIRARD A, GERIG L, PREFONTAINE M, DROUIN P, NAIR RC, STATS M: Prognostic significance of endometrial extension in carcinoma of the cervix. *Gynecol Oncol* 1988; **31:** 301.

KANABUS-KAMINSKA JM, FEELEY M, BIRNBOIM HC: Simultaneous protective and damaging effects of cysteamine on intracellular DNA of leukocytes. *Free Radic Biol Med* 1988; **4:** 141.

LITEPLO RG: DNA (cytosine) methylation in murine and human tumor cell lines treated with S-adenosylhomocysteine hydrolase inhibitors. *Cancer Lett* 1988; **39:** 319.

LITEPLO RG, MUNRO S: DNA methylating capacity in metastatic variants of a human melanoma cell line. *Cancer Lett* 1988; **41:** 191.

LOBREAU AU, RAAPHORST GP, SZEKELY JG: The use of immunostaining to quantify x-ray and heat-induced multiple microtuble organizing centers in normal and transformed cells. *Basic Appl Histochem* 1988; **32:** 263.

LOGAN DM, DANG C-Y, IZAGUIRRE CA, HEUBSCH LB: Kaposi's sarcoma – An in vitro study. Clin Invest Med 1988; **11:** C97.

LOGAN D, FUKS A: Cancer diagnosis in vitro using monoclonal antibodies (immunology series). *In:* Kupchik H, ed. Application of Monoclonal Antibodies to Carcinoembryonic Antigen. New York: Marcel Decker, 1988: 243.

MAROUN JA: Clinical response to trimetrexate as sole therapy in non-small cell lung cancer. *Semin Oncol* 1988; **15(Suppl 2):** 38.

MAROUN JA, NATALE RB, FRANSISCO R: Trimetrexate in combination with cisplatin and etoposide in the treatment of non-small cell lung cancer: A pilot study. *Semin Oncol* 1988; **15(Suppl 2):** 17.

MAZERON JJ, CHASSAGNE D, CROOK J et al: Radiation therapy of carcinomas of the skin, of the nose and nasal vestibule: A report of 1676 cases by the "Groupe European de Curietherapie" (RTO 00509). *Radiother Oncol* 1988; **13:** 165.

MAZERON JJ, CHOPIN D, CROOK J et al: Conservative treatment of T2 carcinoma of bladder using a combination of partial cystectomy and iridium 192 implantation. *J Eur Radiotherapie* 1988; **9:** 73.

MAZERON JJ, CROOK J, CHOPIN D et al: Conservative treatment of bladder carcinoma by partial cystectomy and interstitial iridium 192. *Int J Radiat Oncol Biol Phys* 1988; **15:** 1323.

MONTPETIT VJA, STEWART D, DANCEA S, MIKHAEL N: Pathology of dorsal root ganglia in cis-platinum therapy. *J Neuropathol Exp Neurol* 1988; **47:** 312.

NANJI A, STEWART D, MIKHAEL N: Relationship between urine beta-2-microglobulin and platinum levels during cisplatin treatment. *Clin Biochem* 1988; **21:** 69.

PERRAULT DJ, LOGAN DM, STEWART DJ, BRAMWELL VHC, PATERSON AHG, EISENHAUER EA: Phase II study of flutamide in patients with metastatic breast cancer: A National Cancer Institute of Canada Clinical Trials Group Study. *Invest New Drugs* 1988; **6:** 207.

PERRAULT DJ, TURLEY J, QUIRT I, FELD R: A prospective study of vincristine neuropathy. *Proc Am Soc Clin Oncol* 1988; **7:** A1115. (Abstract)

RAAPHORST GP: Modification of radiation induced neoplastic transformation by radiation in normal and thermotolerant cells. *In:* Sugahara T, Saito M, eds. London: Francis Taylor, 1988: 73.

RAAPHORST GP, AZZAM EI: Evaluation of thermoradiosensitization and transformation in C3H-10T1/2 cells induced into a thermotolerant state. *Int J Hyperthermia* 1988; **3:** 345.

RAAPSHORST GP, AZZAM EI: Poly (ADP-ribose) synthetase inhibitors increase radiation and thermal sensitivity but do not affect thermotolerance. *Radiat Res* 1988; **116:** 442.

RAAPHORST GP, AZZAM EI, FEELEY MM: Potentially lethal radiation damage repair and its inhibition by hyperthermia in normal hamster cells, mouse cells and transformed mouse cells. *Radiat Res* 1988; **113:** 171.

RAAPHORST GP, AZZAM EI, SARGENT M, FEELEY MM: Reduced pH increases recovery of potentially lethal radiation damage leading to in vitro transformation. *Int J Radiat Biol* 1988; **54:** 1031.

RAAPHORST GP, FEELEY MM: Hyperthermia damage and its repair or fixation measured at the cellular level. *In:* Sugahara T, Saito M, eds. London: Francis Taylor, 1988: 181.

RAAPHORST GP, FEELEY MM, DA SILVA VF, DANJOUX CE, GERIG LH: A comparison of radiosensitivity, thermal radiosensitization and repair inhibition in human glioma and other tumor cell lines. *Clin Invest Med* 1988; **11:** C95.

RAAPHORST GP, SZEKELY J: Thermal enhancement of cellular radiation damage: A review of complementary and synergistic effects. *J Scan Elect Microsc* 1988; **2:** 513.

SHEPHERD FA, EVANS WK, FELD R, YOUNG V, PATTERSON GA, GINSBURG R, JOHANSEN E: Adjuvant chemotherapy following surgical resection for small cell carcinoma of lung. *J Clin Oncol* 1988; **6:** 832.

SHEPHERD FA, EVANS WK, GARVEY B, READ SE, KLEIN M, FANNING M, COATES R: Combination chemotherapy and interferon in the treatment of Kaposi's sarcoma associated with acquired immune deficiency syndrome. *Can Med Assoc* J 1988; **139:** 635.

SHEPHERD FA, EVANS WK, KUTAS G, YAU JC, DANG P, SCOTT JG, FARQUHARSON HA, FRANCOMBE WH, BAILEY D, BAKER MA: Chemotherapy following surgery for Stages IE and IIE non-Hodgkin's lymphoma of the gastrointestinal tract. *J Clin Oncol* 1988; **6:** 253.

SHEPHERD FA, GINSBURG R, EVANS WK, PATTERSON G, FELD R: Neoadjuvant chemotherapy followed by surgery for limited small-cell lung cancer. *Lung Cancer* 1988; **4(Suppl):** A153. (Abstract 8.1.04)

SHEPHERD FA, GINSBURG R, PATTERSON G, EVANS WK, FELD R: Adjuvant chemotherapy after surgery for limited small-cell lung cancer. *Lung Cancer* 1988; **4(Suppl):** A153. (Abstract 8.1.03)

STEWART D, DANCEA S, MIKHAEL N, MONTPETIT VJA, KEANEY MA, TRYPHONAS L: The effects of cisplatinum on ferret dorsal root ganglia. *J Neuropathol Exp Neurol* 1988; **47:** 312. (Abstract)

STEWART DJ, MIKHAEL NZ, NAIR RC, KACEW S, MONTPETIT V, NANJI A, MAROUN JA, HOWARD K: Platinum concentrations in human autopsy tumor samples. *Am J Clin Oncol* 1988; **11:** 152.

STEWART DJ, VERMA S, MAROUN J: Phase I study of weekly oral menogaril. *Proc Am Soc Clin Oncol* 1988; **7:** 57.

STEWART DJ, VERMA S, MAROUN J: Phase I study of daily x 3 oral idarubicin. *Proc Am Assoc Cancer Res* 1988; **29:** 221. (Abstract)

VENNER PM, KLOTZ PG, KLOTZ LH, STEWART DJ, DAVIS IR, OROVAN WL, RAMSEY ER: Megestrol acetate plus minidose diethylstilbestrol in the treatment of carcinoma of the prostate. *Semin Oncol* 1988; **15:** 62.

WEINERMAN B, MAROUN J, STEWART D, CRIPPS C, JOHNSTON J: Sequential methotrexate, 5-fluorouracil and leucovorin in metastatic measurable colorectal cancer. Does it work? *Clin Invest Med* 1988; **11(Suppl):** C92. (Abstract)

WEINERMAN B, MAROUN JA, STEWART D, CRIPPS C, JOHNSTON J: Sequential methotrexate (M), 5-fluorouracil (F) & leucovorin (L) in metastatic measurable colorectal cancer (CRC). *Proc Soc Clin Oncol* 1988; **7:** 102. (Abstract 392)

SUDBURY

Northeastern Ontario Oncology Program:

GOSS GD, VINCENT MD, GERMOND C, SINOFF CL, BOZEK T, KANE G, CORRINGHAM R: Teniposide (VM26) and carboplatinum (CP) for small cell lung cancer (SCLC). *Proc Am Soc Clin Oncol* 1988; **7:** 216. (Abstract 837)

SINOFF CL, BLUMSOHN A: Spinal cord compression in myelomatosis: Response to chemotherapy alone. *Eur J Cancer Clin Oncol* 1988; **25:** 197.

VINCENT MD, EVANS BD, SMITH IE: First-line chemotherapy re-challenge after relapse in small cell lung cancer. *Cancer Chemother Pharmacol* 1988; **21:** 45.

VINCENT MD, GOSS GD, SINOFF CL, BOZEK T, KANE G, CORRINGHAM R: Teniposide (VM 26) and paraplatin (CBDCA) in small cell lung cancer (SCLC). *Lung Cancer* 1988; **4(Suppl):** A116. (Abstract 6.1.68)

THUNDER BAY

OCTRF Thunder Bay Regional Cancer Centre:

AL-GHAZI MSAL, ARJUNE B, FIEDLER JA, SHARMA PD: Dosimetric aspects of the therapeutic photon beams from a dual energy linear accelerator. *Med Phys* 1988; **15:** 250.

TORONTO

Ontario Cancer Institute:

ADAMS F: Emergency intravenous sedation of the delirious, medically ill patient. *J Clin Psychiatry* 1988; **49(Suppl):** 22.

ADAMS F: Neuropsychiatric evaluation and treatment of delirium in cancer patients. *Adv Psychosom Med* 1988; **18:** 26.

ADDLEMAN M, ERLICHMAN C, WARR D, FINE S, MURRAY C: Phase I: Trial of BRL43694, a 5-HT3 antagonist in the prevention of chemotherapy induced nausea and vomiting. *Proc Am Soc Clin Oncol* 1988; **7:** A297. (Abstract)

ALTARAS MM, GOLDBERG GL, LEVIN W, BLOCH B, DARGE L, SMITH JA: The role of cancer antigen 125 (CA 125) in the management of ovarian epithelial carcinoma. *Gynecol Oncol* 1988; **30:** 26.

ARSENAULT AL, LING V, KARTNER N: Altered plasma membrane ultrastructure in multidrug-resistant cells. *Biochim Biophys Acta* 1988; **938:** 315.

ARSENAULT AL, OTTENSMEYER FP, HEALTH IB: An electron microscopic and spectroscopic study of murine epithelial cartilage: Analysis of fine structure and matrix vesicles preserved by slam freezing and freeze substitution. *J Ultrastruct Mol Struct Res* 1988; **98:** 32.

BALLHAUSEN WG, RESKE-KUNZ AB, TOURVIEILLE B, OHASHI PS, PARNES JR, MAK TW: Acquisition of an additional antigen specificity after mouse CD4 gene transfer into a T helper hybridoma. *J Exp Med* 1988; **167:** 1493.

BECKER JB, ADAMS F, ROBINSON TE: Intraventricular microdialysis: A new method for determining monoamine metabolite concentrations in the cerebrospinal fluid of freely moving rats. *J Neurosci Methods* 1988; **24:** 259.

BEN-DAVID Y, PRIDEAUX VR, CHOW V, BENCHIMOL S, BERNSTEIN A: Inactivation of the p53 oncogene by internal deletion or retroviral integration in erythroleukemic cell lines induced by Friend leukemia virus. *Oncogene* 1988; **3:** 179.

BENVENISTE P, DERRY H, WU GE, PAIGE CJ, MILLER RG: A sensitive dot blot procedure for detecting mRNA in lymphoid cells grown in liquid culture. *J Immunol Methods* 1988; **107:** 165.

BERGERON MG, MENDELSON J, HARDING GK, MANDELL L, FONG IW, RACHLIS A, CHAN R, BIRON S, FELD R, SEGAL NB: Cefoperazone compared with ampicillin plus tobramycin for severe biliary tract infections. *Antimicrob Agents Chemother* 1988; **32:** 1231.

BERGSAGEL DE: Chemotherapy of myeloma: Drug combinations versus single agents, an overview, and comments on acute leukemia in myeloma. *Hematol Oncol* 1988; **6:** 159.

BERGSAGEL DE: Interferon alfa-2b in the management of chronic granulocytic leukemia. *Cancer Treat Rev* 1988; **15(Suppl A):** 15.

BERGSAGEL DE: Use of gentle approach for refractory myeloma patients. *Clin Oncol* 1988; **6:** 767. (Editorial)

BERSTEIN M, LAPPERRIERE N, McKENZIE S, LEUNG P: Complications of interstitial brachytherapy in patients with malignant astrocytomas. *Can J Neurol Sci* 1988; **15:** 227. (Abstract)

BISSETT RJ, FITZPATRICK PJ: Malignant submandibular gland tumors: A review of 91 patients (published erratum appears in Am J Clin Oncol 1988 Aug; **11:** 514). *Am J Clin Oncol* 1988; **11:** 46.

BOUX LJ, MILLIGAN JR, ARCHER MC: Base-catalysed decomposition of N-nitrosobis(2-oxopropyl)amine. *Chem Res Toxicol* 1988; **1:** 32.

BOXEN I: Intense bilateral breast uptake of gallium-67. *J Nucl Med* 1988; **29:** 1606. (Letter)

BOYD NF: Diet and cyclical mastopathy. *Lancet* 1988; 2: 914. (Letter)

BOYD NF, COUSINS M, BEATON M, FISHELL E, WRIGHT B, FISH E, KRIUKOV V, LOCKWOOD G, TRITCHLER D, HANNA W et al: Clinical trial of low-fat, high-carbohydrate diet in subjects with mammographic dysplasia: Report of early outcomes. *J Natl Cancer Inst* 1988; **80:** 1244.

BOYD NF, McGUIRE V, SHANNON P, COUSINS M, KRIUKOV V, MAHONEY L, FISH E, LICKLEY L, LOCKWOOD G, TRITCHLER D: Effect of low-fat high-carbohydrate diet on symptoms of clinical mastopathy. *Lancet* 1988; **2:** 128.

BOYD NF, SELBY PJ, SUTHERLAND HJ, HOGG S: Measurement of the clinical status of patients with breast cancer: Evidence for the validity of self assessment with linear analogue scales. *J Clin Epidemiol* 1988; **41:** 243.

BRADLEY G, JURANKA PF, LING V: Mechanism of multidrug resistance. *Biochim Biophys Acta* 1988; **948:** 87.

BRADY G, WILLIAMS RL, NORDSTROM K, VENNSTROM B, COURTNEIDGE SA, WAGNER EF, GRAF T, ISCOVE NN: A selectable temperature-sensitive v-src Moloney retrovirus. *Oncogene* 1988; **3:** 687.

BRONSKILL MJ, HENKELMAN RM, POON PY, EGE GN, DUNLAP HJ, HO CS, GOLDFINGER M, TAYLOR BR, STONE RM, SUTCLIFFE SB et al: Magnetic resonance imaging, computed tomography, and radionuclide scintigraphy in detection of liver metastases. *J Can Assoc Radiol* 1988; **39:** 3.

BRONSKILL MJ, McVEIGH ER, KUCHARCZYK W, HENKELMAN RM: Syrinx-like artifacts on MR images of the spinal cord. *Radiology* 1988; **166:** 485.

CACCIA M, MAK TW: T cell receptors. *Am J Med* 1988; **85:** 9.

CATZ-BIRO L, MILLIGAN JR, CHIN W, GILES A, CHUI YC, ARCHER MC: Comparative cytotoxicity of n-nitrosodimethylamine and n-nitrosomethyl-benzylamine in rat liver and cultured hepatocytes. *Proc Am Assoc Cancer Res* 1988; **29:** A340. (Abstract)

CHAMPAGNE E, SAGMAN U, BIONDI A, LEWIS WH, MAK TW, MINDEN MD: Structure and rearrangement of the T cell receptor J alpha locus in T cells and leukemic T cell lines. *Eur J Immunol* 1988; **18:** 1033.

CHAMPAGNE E, TAKIHARA Y, SAGMAN U, BURROW S, de SOUSA J, MAK TW, MINDEN MD: The isolation of the human delta chain gene and its expression in normal T cells and T cell leukemias. *Leukemia* 1988; **2:** 717.

CHAN HS, BRADLEY G, THORNER P, HADDAD G, GALLIE BL, LING V: A sensitive method for immunocytochemical detection of P-glycoprotein in multidrug-resistant human ovarian carcinoma cell lines. *Lab Invest* 1988; **59:** 870.

CHAN HS, GALLIE B, THORNER P, HADDAD G, BRADLEY G, LING V: Immunocytochemical diagnosis of P-glycoprotein-related multidrug resistance in retinoblastoma. *Proc Am Assoc Cancer Res* 1988; **29:** A1229. (Abstract)

CHENG GY, KELLEHER CA, MIYAUCHI J, WANG C, WONG G, CLARK SC, McCULLOCH EA, MINDEN MD: Structure and expression of genes of GM-CSF and G-CSF in blast cells from patients with acute myeloblastic leukemia. *Blood* 1988; **71:** 204.

CHURCH JG, BUICK RN: G-protein-mediated epidermal growth factor signal transduction in a human breast cancer cell line: Evidence for two intracellular pathways distinguishable by pertussis toxin. *J Biol Chem* 1988; **263:** 4242.

CIAMPI A, LOCKWOOD G, SUTHERLAND HJ, LLEWELLYN-THOMAS HA, TILL JE: Assessment of health-related quality of life: Factor scales for patients with breast disease. *J Psychosoc Oncol* 1988; **6:** 1.

COCKSHUTT JR, SCHATZKER J, SUMNER-SMITH G, FORNASIER VL: Biological fixation of a porous coated metal backed acetabular component in canine total hip arthroplasty. *Vet Comp Orthop Tramatol* 1988; **3:** 141.

COURNOYER D, BEAUCHEMIN N, BOUCHER D, BENCHIMOL S, FUKS A, STANNERS CP: Transcription of genes of the carcinoembryonic antigen family in malignant and nonmalignant human tissues. *Cancer Res* 1988; **48:** 3153

CRAWLEY AP, HENKELMAN RM: A comparison of one-shot and recovery methods in T1 imaging. *Magn Reson Med* 1988; **7:** 23.

CRAWLEY AP, WOOD ML, HENKELMAN RM: Elimination of transverse coherences in FLASH MRI. *Magn Reson Med* 1988; **8:** 248.

CUNNINGHAM AJ: A new medical theory: Infomedicine. *Advances* 1988; **5:** 33.

CUNNINGHAM AJ: An evaluation of cognitive behaviour therapy for the relief of psychological distress in cancer patients. *Diss Abstr Int* (A) 1988; **48:** 2577.

CUNNINGHAM AJ: From neglect to support to coping: The evolution of psychosocial intervention for cancer patients. *In:* Cooper CL, ed. Stress and Breast Cancer. New York: John Wiley and Sons, 1988; 135.

CUNNINGHAM JR: Dosimetric principles. *Radiographics* 1988; **8:** 785.

DULHANTY AM, RUBIN JS, WHITMORE GF: Complementation of the DNA-repair defect in a CHO mutant by human DNA that lacks highly abundant repetitive sequences. *Mutat Res* 1988; **194:** 207.

EPSTEIN J, BARLOGIE B, LING V: VAD resistant tumor cells in aneuploid multiple myeloma (MM) over-express MDR$_1$-associated P-glycoprotein. *Proc Am Assoc Cancer Res* 1988; **29:** A1198. (Abstract)

ERLICHMAN C, FINE S, WONG A, ELHAKIM T: A randomized trial of fluorouracil and folinic acid in patients with metastatic colorectal carcinoma. *J Clin Oncol* 1988; **6:** 469.

ERLICHMAN C, SOLDIN SJ, HARDY RW, THIESSEN JJ, STURGEON JF, FINE S, BASKERVILLE T: Disposition of cyclophosphamide on two consecutive cycles of treatment in patients with ovarian carcinoma. *Arzneimittelforschung* 1988; **38:** 839.

ERLICHMAN C, WU A: Penetration and cytotoxicity of 5-fluorouracil (5-FU) in MGH-U1 multicellular spheroids (MTS). *Proc Am Assoc Cancer Res* 1988; **29:** A1399. (Abstract)

FARROW NA, OTTENSMEYER FP: Maximum entropy methods in dark field micrographs and elemental maps. *Scann Microsc* 1988; **Suppl 2:** 75.

FARROW NA, OTTENSMEYER FP: Towards a method of correcting bias introduced by the error fitting model in conjunction with a maximum entropy processing algorithm. *In:* Erickson GJ, Smith CR, eds. Maximum-Entropy and Baysian Methods in Science and Engineering, Vol. 2. Hingham, MASS: Kluwer Academic Publishers, 1988: 313.

FEIGEN M, CUMMINGS BJ, HAWKINS N, KEAN TJ, O'SULLIVAN B, WONG CS: Low dose postoperative adjuvant radiation therapy for rectal cancer is ineffective. *Radiother Oncol* 1988; **13:** 181.

FELD R, DeBOER G, SAGMAN U: Prognostic factors for small cell carcinoma of the lung. *Eur J Cancer Clin Oncol* 1988; **24:** 353.

FELD R, PATER J, COY P: Restaging of responding patients (PTS) with limited disease (LD) small cell lung cancer (SCLC) – is it really necessary? Proc Am Soc Clin Oncol 1988; **7:** A785. (Abstract)

FELD R, WIERZBICKI R, WALDE D, SHEPHERD F, EVANS WK, BURKES R, HOLLOWAY C, LASSUS M: High dose epirubicin (E) given as a daily x 3 schedule in patients (PTS) with untreated extensive non-small cell lung cancer (NSCLC): A Phase I-II study. *Proc Am Assoc Cancer Res* 1988; **29:** A826. (Abstract)

FELLER AC, GRIESSER H, SCHILLING CV, WACKER HH, DALLENBACH F, BARTELS H, KUSE R, MAK TW, LENNERT K: Clonal gene rearrangement patterns correlate with immunophenotype and clinical parameters in patients with angioimmunoblastic lymphadenopathy. *Am J Pathol* 1988; **133:** 549.

FERNANDEZ F, ADAMS F, LEVY JK, HOLMES VF, NEIDHART M, MANSELL PW: Cognitive impairment due to AIDS-related complex and its response to psychostimulants. *Psychosomatics* 1988; **29:** 38.

FERNANDEZ F, HOLMES VF, ADAMS F, KAVANAUGH JJ: Treatment of severe, refractory agitation with a haloperidol drip. *J Clin Psychiatry* 1988; **49:** 239.

FIGLIN RA, PIANTADOSI S, FELD R: Intracranial recurrence of carcinoma after complete surgical resection of Stage I, II, and III non-small-cell lung cancer. *N Engl J Med* 1988; **318:** 1300.

FILMUS J, CHURCH JG, BUICK RN: Isolation of a cDNA corresponding to a developmentally regulated transcript in rat intestine. *Mol Cell Biol* 1988; **8:** 4243.

FINE S, ERLICHMAN C, KAIZER L, WARR D, ELHAKIM T: Phase II trial of 5FU + folinic acid (FA) as first line treatment for metastatic breast cancer. *Proc Am Soc Clin Oncol* 1988; **7:** A161. (Abstract)

FREDERICKS WJ, MURAWSKI MJ, SLOCUM HK, GERLACH JH, LING V, BAKER RM: Incidence of elevated P-glycoprotein expression in human tumors. *Proc Am Assoc Cancer Res* 1988; **29:** A1200. (Abstract)

GANNON M: Preventing emesis in cancer patients. *N Z Pharmacy* 1988; **8:** 30.

GILBERT RW, LUNDGREN JA, van NOSTRAND AW, KEANE TJ: T3NOMO glottic carcinoma – a pathologic analysis of 41 patients treated surgically following radiotherapy. *Clin Otolaryngol* 1988; **13:** 467.

GILCHRIST D, CHAN CK, LAROYE GJ, MESSNER HA, CURTIS JE: Bronchial mucosal infiltration and unilateral lung collapse: An unusual complication of multiple myeloma. *Am J Med* 1988; **85:** 740.

GOLDBERG H, LING V, WONG PY, SKORECKI K: Reduced cyclosporin accumulation in multidrug-resistant cells. *Biochem Biophys Res Commun* 1988; **152:** 552.

GOODMAN SB, FORNASIER VL, KEI J: The effects of bulk versus particulate ultra-high-molecular-weight polyethylene on bone. *J Arthroplasty* 1988; **3(Suppl):** S41.

GOODMAN SB, FORNASIER VL, KEI J: The effects of bulk versus particulate polymethylmethacrylate on bone. *Clin Orthop* 1988; **232:** 255.

GOODWIN PJ, BOYD NF: Mammographic parenchymal pattern and breast cancer risk: A critical appraisal of the evidence. *Am J Epidemiol* 1988; **127:** 1097.

GOODWIN PJ, FELD R, EVANS WK, PATER J: Cost-effectiveness of cancer chemotherapy: An economic evaluation of a randomized trial in small-cell lung cancer. *J Clin Oncol* 1988; **6:** 1537.

GOODWIN PJ, NEELAM M, BOYD NF: Cyclical mastopathy: A critical review of therapy. *Br J Surg* 1988; **75:** 837.

GOODWIN PJ, PANZARELLA T, BOYD NF: Weight gain in women with localized breast cancer – a descriptive study. *Breast Cancer Res Treat* 1988; **11:** 59.

GORCZYNSKI RM: Effect of neonatal injection with antibodies to Leishmania mexicana on its growth in adult infected mice. *Infect Immun* 1988; **56:** 1376.

GRAHAM KA, BUICK RN: Sodium butyrate induces differentiation in breast cancer cell lines expressing the estrogen receptor. *J Cell Physiol* 1988; **136:** 63.

GREENBERGER LM, WILLIAMS SS, GEORGES E, LING V, HORWITZ SB: Electrophoretic analysis of P-glycoproteins produced by mouse J774.2 and Chinese hamster ovary multidrug-resistant cells. *J Natl Cancer Inst* 1988; **80:** 506.

GRIESSER H, CHAMPAGNE E, TKACHUK D, TAKIHARA Y, LALANDE M, BAILLIE E, MINDEN M, MAK TW: The human T cell receptor alpha-delta locus: A physical map of the variable, joining and constant region genes. *Eur J Immunol* 1988; **18:** 641.

GRIESSER H, MAK TW: Immunogenotyping in Hodgkin's disease. *Hematol Oncol* 1988; **6:** 239.

GRIFFIN TW, PAJAK TF, LARAMORE GE, DUNCAN W, RICHTER MP, HENRICKSON FR, MAOR MH: Neutron vs photon irradiation of inoperable salivary gland tumors: Results of an RTOG-MRC Cooperative Randomized Study. *Int J Radiat Oncol Biol Phys* 1988; **15:** 1085.

GRONOSTAJSKI RM, KNOX J, BERRY D, MIYAMOTO NG: Stimulation of transcription in vitro by binding sites for nuclear factor I. *Nucleic Acids Res* 1988; **16:** 2087.

GUNHOUSE BW, MILLIGAN JR, ARCHER MC: Interaction of alpha-acetoxy-N-nitrosopyrrolidine with DNA assessed by loss of restriction endonuclease recognition sites and formation of apurinic/apyrimidinic sites. *Carcinogenesis* 1988; **9:** 1595.

HARA J, BENEDICT SH, CHAMPAGNE E, MAK TW, MINDEN M, GELFAND EW: Comparison of T cell receptor alpha, beta, and gamma gene rearrangement and expression in T cell acute lymphoblastic leukemia. *J Clin Invest* 1988; **81:** 989.

HARA J, BENEDICT SH, CHAMPAGNE E, TAKIHARA Y, MAK TW, MINDEN M, GELFAND EW: T cell receptor delta gene rearrangments in acute lymphoblastic leukemia. *J Clin Invest* 1988; **82:** 1974.

HENKELMAN RM, MESSNER H, POON PY, HINKS RS, STEWART C, CURTIS J, MINDEN M, BAKER M: Magnetic resonance imaging for monitoring relapse of acute myeloid leukemia. *Leuk Res* 1988; **12:** 811.

HINKS RS, HENKELMAN RM: Problems with organic materials for magnetic resonance imaging phantoms. *Med Phys* 1988; **15:** 61.

HORWICH A, CATTON CN, QUIGLEY M, EASTON D, BRADA M: The management of early-stage aggressive non-Hodgkin's lymphoma. *Hematol Oncol* 1988; **6:** 291.

ISCOVE NN, FAGG B, KELLER G: A soluble activity from adherent marrow cells cooperates with IL3 in stimulating growth of pluripotential hematopoietic precursors. *Blood* 1988; **71:** 953.

JACOBS BL, MIYAMOTO NG, SAMUEL CE: Mechanism of interferon action: Studies on the activation of protein phosphorylation and the inhibition of translation in cell-free systems. *J Interferon Res* 1988; **8:** 617.

JEWETT MA, KONG YS, GOLDBERG SD, STURGEON JF, THOMAS GM, ALISON RE, GOSPODAROWICZ MK: Retroperitoneal lymphadenectomy for testis tumor with nerve sparing for ejaculation. *J Urol* 1988; **139:** 1220.

KAIZER L, FISHELL EK, HUNT JW, FOSTER FS, BOYD NF: Ultrasonographically defined parenchymal patterns of the breast: Relationship to mammographic patterns and other risk factors for breast cancer. *Br J Radiol* 1988; **61:** 118.

KELLEHER CA, WONG GG, CLARK SC, SCHENDEL PF, MINDEN MD, McCULLOCH EA: Binding of iodinated recombinant human GM-CSF to the blast cells of acute myeloblastic leukemia. *Leukemia* 1988; **2:** 211.

KEYSTONE EC, MINDEN M, CLARK R, POPLONSKI L, ZALCBERG J, TAKADERA T, MAK TW: Structure of T cell antigen receptor beta chain in synovial fluid cells from patients with rheumatoid arthritis. *Arthritis Rheum* 1988; **31:** 1555.

KEYSTONE EC, POPLONSKI L, MILLER RG, GORCZYNSKI R, GLADMAN D, SNOW K: Reactivity of T-cells from patients with rheumatoid arthritis to anti-CD3 antibody. *Clin Immunol Immunopathol* 1988; **48:** 325.

KOGA Y, KIMURA N, MINOWADA J, MAK TW: Expression of the human T-cell-specific tyrosine kinase YT16 (LCK) message in leukemic T-cell lines. *Cancer Res* 1988; **48:** 856.

KOGA Y, LINDSTROM E, FENYO EM, WIGZELL H, MAK TW: High levels of heterodisperse RNAs accumulate in T cells infected with human immunodeficiency virus and in normal thymocytes. *Proc Natl Acad Sci USA* 1988; **85:** 4521.

KOVNAT A, BUICK RN, CHOO B, De HARVEN E, KOPELYAN I, TRENT JM, TANNOCK IF: Malignant properties of sublines selected from a human bladder cancer cell line that contains an activated c-Ha-ras oncogene. *Cancer Res* 1988; **48:** 4993.

KROEKER RM, STEWART CA, BRONSKILL MJ, HENKELMAN RM: Continuous distributions of NMR relaxation times applied to tumors before and after therapy with X-rays and cyclophosphamide. *Magn Reson Med* 1988; **6:** 24.

KUCHARCZYK W, CRAWLEY AP, KELLY WM, HENKELMAN RM: Effect of multislice interference on image contrast in T2- and T1-weighted MR images. *AJNR* 1988; **9:** 443.

LADEROUTE K, WARDMAN P, RAUTH AM: Molecular mechanisms for the hypoxia-dependent activation of 3-amino-1,2,4-benzotriazine-1,4-dioxide (SR 4233). *Biochem Pharmacol* 1988; **37:** 1487.

LAPERRIERE NJ, BERNSTEIN M: Removal of malignant astrocytomas. *Neurosurgery* 1988; **22:** 440. (Letter)

LI KC, POON PY: Sensitivity and specificity of MRI in detecting malignant spinal cord compression and in distinguishing malignant from benign compression fractures of vertebrae. *Magn Reson Imag* 1988; **6:** 547.

LING V: Multidrug resistance and P-glycoprotein expression in biological approaches to the controlled delivery of drugs. *Ann N Y Acad Sci* 1988: **507:** 7.

LING V, JURANKA PF, ENDICOTT JA, DEUCHARS KL, GERLACH JH: Multidrug resistance and P-glycoprotein expression in mechanisms of drug resistance in neoplastic cells. *Bristol-Myers Cancer Symposia* 1988: **9:** 197.

LISHNER M, PERRIN R, FELD R, ALHAKIM T, MESSNER H, TUFFNELL P, MATLOW A, CURTIS J: Complications associated with ommaya reservoirs in patients with cancer. *Proc Am Soc Clin Oncol* 1988: **7:** A1106. (Abstract)

LLEWELLYN-THOMAS HA, McGREAL MJ, THIEL EC, ERLICHMAN C, FINE S: Patients' willingness to enter clinical trials: The association with perceived benefit and decision making preference. *Med Decis Making* 1988: **8:** 337. (Abstract)

LLEWELLYN-THOMAS HA, SUTHERLAND JH, TIBSHIRANI R, CIAMPI A, TILL JE, BOYD NF: The measurement of patients values in medicine. *In:* Dowie J, Elstein A, eds. Professional Judgment: A Reader in Clinical Decision Making. Cambridge: Cambridge University Press, 1988: 395.

LLEWELLYN-THOMAS HA, THIEL EC, CLARK RM: Patients vs surrogates: Whose opinion counts on ethics review panels? *Med Decis Making* 1988: **8:** 336. (Abstract)

LUK CK, TANNOCK IF: Tumour response to chemotherapy in animals that have been treated with the same drugs prior to tumour implantation: A model for studying host effects on apparent drug resistance. *Br J Cancer* 1988: **58:** 133.

LUNDGREN JA, GILBERT RW, van NOSTRAND AW, HARWOOD AR, KEANE TJ, BRIANT TD: T3NOMO glottic carcinoma – a failure analysis. *Clin Otolaryngol* 1988: **13:** 455.

MAH K, Van DYK J: Quantitative measurement of changes in human lung density following irradiation. *Radiother Oncol* 1988: **11:** 169.

MAK I, MAK S, BENCHIMOL S: Expression of the cellular p53 protein in cells transformed by adenovirus 12 and viral DNA fragments. *Virology* 1988: **163:** 201.

MARSHALL RS, RAUTH AM: Oxygen and exposure kinetics as factors influencing the cytotoxicity of porfiromycin, a mitomycin C analogue, in Chinese hamster ovary cells. *Cancer Res* 1988; **48:** 5655.

McCULLOCH EA, KELLEHER CA, MIYAUCHI J, WANG C, CHENG GY, MINDEN MD, CURTIS JE: Heterogeneity in acute myeloblastic leukemia. *Leukemia* 1988; **2(12 Suppl):** 38S.

McVEIGH ER, BRONSKILL MJ, HENKELMAN RM: Optimization of MR protocols: A statistical decision analysis approach. *Magn Reson Med* 1988; **6:** 314.

MILLER RG, MURAOKA S, CLAESSON MH, REIMANN J, BENVENISTE P: The veto phenomenon in T-cell regulation. *Ann N Y Acad Sci* 1988; **532:** 170.

MILLIGAN JR, ARCHER MC: Alkylation of individual genes in rat liver by the carcinogen N-nitrosodimethylamine. *Biochem Biophys Res Commun* 1988; **155:** 14.

MILLIGAN JR, CATZ-BIRO L, HIRANI-HOJATTI S, ARCHER MC: Interaction of activated N-nitrosamines with DNA. *In:* Feo F, Pani P, Columbano A, Garcea R, eds. Models and Mechanisms in Chemical Carcinogenesis. New York: Plenum Press, 1988: 111.

MITCHELL SA: Living as a women after cancer. *Can Med Assoc J* 1988; **139:** 1165.

MIYAUCHI J, KELLEHER CA, WONG GG, YANG YC, CLARK SC, MINKIN S, MINDEN MD, McCULLOCH EA: The effects of combinations of the recombinant growth factors GM-CSF, G-CSF, IL-3, and CSF-1 on leukemic blast cells in suspension culture. *Leukemia* 1988; **2:** 382.

MIYAUCHI J, WANG C, KELLEHER CA, WONG GG, CLARK SC, MINDEN MD, McCULLOCH EA: The effects of recombinant CSF-1 on the blast cells of acute myeloblastic leukemia in suspension culture. *J Cell Physiol* 1988; **135:** 55.

MOORE MJ, HARDY RW, THIESSEN JJ, SOLDIN SJ, ERLICHMAN C: Rapid development of enhanced clearance after high-dose cyclophosphamide. *Clin Pharmacol Ther* 1988; **44:** 622.

MOORE MJ, O'SULLIVAN B, TANNOCK IF: How expert physicians would wish to be treated if they had genitourinary cancer. *J Clin Oncol* 1988; **6:** 1736.

MOORE MJ, TANNOCK IF: How expert physicians would wish to be treated if they developed genito-urinary cancer. *Proc Am Soc Clin Oncol* 1988; **7:** A455. (Abstract)

MUNRO P, RAWLINSON JA, FENSTER A: Therapy imaging: Source size of radiotherapy beams. *Med Phys* 1988; **15:** 517.

MUNROE DG, ROVINSKI B, BERNSTEIN A, BENCHIMOL S: Loss of a highly conserved domain on p53 as a result of gene deletion during Friend virus-induced erythroleukemia. *Oncogene* 1988; **2:** 621.

MURAOKA S, MILLER RG: The autoimmune mouse MRL/Mp-lpr/lpr contains cells with spontaneous cytotoxic activity against target cells bearing self-determinants. *Cell Immunol* 1988; **113:** 20.

NG W, SARANGI F, ZASTAWNY R, LING V: The hamster P-glycoprotein gene family contains three members: pgp1, pgp2 and pgp3. *Proc Am Assoc Cancer Res* 1988; **29:** A1226. (Abstract)

NOSS MB, PANICUCCI R, McCLELLAND RA, RAUTH AM: Preparation toxicity and mutagenicity of 1-methyl-2-nitrosoimidazole: A toxic 2-nitroimidazole reduction product. *Biochem Pharmacol* 1988; **37:** 2585.

O'SULLIVAN B: Limb-sparing management in extremity soft-tissue sarcomas in the adult: The radiation oncologist's viewpoint. *Can J Surg* 1988; **31:** 397.

OKADA A, BANK I, ROGOZINSKI L, TAKIHARA Y, MAK TW, CHESS L, ALT FW: Structure of the gamma/delta T cell receptor of a human thymocyte clone. *J Exp Med* 1988; **168:** 1481.

OSOBA D, ERLICHMAN C, WILLAN AR, BRIGDEN ML, GEGGIE P, PATER JL, RUSTHOVEN JJ, WILSON KS: Failure of methylprednisolone acetate to prolong the antinauseant effect of intravenous methylprednisolone sodium succinate in patients receiving chemotherapy. *Clin Invest Med* 1988; **11:** 377.

OTTENSMEYER FP, ANDREWS DW, ARSENAULT AL, HENG YM, SIMON GT, WEATHERLY GC: Elemental imaging by electron energy loss microscopy. *Scanning* 1988; **10:** 227.

OTTENSMEYER FP, FRANKLAND BW: Spectral processing for parallel recording of elemental maps. *Scann Microsc* 1988; **Suppl 2:** 343.

PAYNE DG: Non-small cell lung cancer: Should unresectable Stage III patients routinely receive high-dose radiation therapy? *J Clin Oncol* 1988; **6:** 552.

PAYNE DG, FELD R: Concurrent radiotherapy and chemotherapy in lung cancer at the Princess Margaret Hospital. *Antibiot Chemother* 1988; **41:** 96.

POON PY, McCALLUM RW, HENKELMAN RM, BRONSKILL MJ, DUNLAP HJ, SUTCLIFFE SB, GOSPODAROWICZ M, STONE RM, WILLIAMS JI: MRI of periprostatic venous plexus in staging of early prostatic carcinoma. *J Can Assoc Radiol* 1988; **39:** 111.

PROST JL, WEHRLI FS, DRAYER D, FROELICH J, HEARSHEN D, PLEWES DB: SA reduced pulse sequences. *Magn Reson Imag* 1988; **6:** 1.

REIS MD, MAK TW: Monoclonality in human T-cell disorders. *Blood Rev* 1987; **1:** 89.

RENICK B, CLARK RM, FELDMAN L: Embryonal rhabdomyosarcoma: Presentation as a parotid gland mass. *Oral Surg Oral Med Oral Pathol* 1988; **65:** 575.

ROSEN IB, SUTCLIFFE SB, GOSPODAROWICZ MK, CHUA T, SIMPSON WJ: The role of surgery in the management of thyroid lymphoma. *Surgery* 1988; **104:** 1095.

ROVINSKI B, BENCHIMOL S: Immortalization of rat embryo fibroblasts by the cellular p53 oncogene. *Oncogene* 1988; **2:** 445.

SAGMAN U, FELD R, DeBOER G, CIAMPI A, EVANS WK, SHEPHERD F, WARR D, MALKIN A, GINSBERG R: Long term survival of patients (PTS) with small cell lung cancer (SCLC) – the Toronto experience (1976-1986). *Proc Am Soc Clin Oncol* 1988; **7:** A786. (Abstract)

SANTYR GE, HENKELMAN RM, BRONSKILL MJ: Variation in measured transverse relaxation in tissue resulting from spin locking with the CPWG sequence. *J Magn Reson* 1988; **79:** 28.

SAUTER H, PAIGE CJ: B cell progenitors have different growth requirements before and after immunoglobulin heavy chain commitment. *J Exp Med* 1988; **168:** 1511.

SHEPHERD F, GINSBERG R, PATTERSON G, EVANS W, FELD R: Combined modality therapy including surgery for small cell lung cancer (SCLC): The Toronto Lung Oncology Group experience. *Proc Am Soc Clin Oncol* 1988; **7:** A758. (Abstract)

SILBERFELD M, PHOENIX C, LOCKWOOD G, TRITCHLER D, TILL JE: Choosing a risky treatment. *Psychiatr J Univ Ottawa* 1988; **13:** 9.

SIMON J, SZUMOWSKI J, TOTTERMAN S, KIDO D, EKHOLM S, WICKS, A, PLEWES DB: Fat suppression magnetic resonance imaging of the orbit. *AJRN* 1988; **9:** 961.

SIMPSON WJ, CARRUTHERS J: Squamous cell carcinoma of the thyroid gland. *Am J Surg* 1988; **156:** 44.

SIMPSON WJ, PANZARELLA T, CARRUTHERS JS, GOSPODAROWICZ MK, SUTCLIFFE SB: Papillary and follicular thyroid cancer: Impact of treatment in 1578 patients. *Int J Radiat Oncol Biol Phys* 1988; **14:** 1063.

SLOVAK M, LING V, TRENT J: Molecular /cytogenetic characterization of the sequential development of multidrug resistance (MDR) in a panel of colchicine resistant (CLCR) cell lines. *Proc Am Assoc Cancer Res* 1988; **29:** A1270. (Abstract)

SMITH LJ, BENCHIMOL S: Introduction of new genetic material into human myeloid leukemic blast stem cells by retroviral infection. *Mol Cell Biol* 1988; **8:** 974.

SOUZA SP, DUMOULIN CR, SZUMOWSKI J, PLEWES DG, GLOVER G: A simultaneous multislice acqisition method for magnetic resonance imaging. *J Comput Assist Tomogr* 1988; **12:** 1026.

SPOLSKI R, MIESCHER G, ERARD F, RISSER R, MacDONALD HR, MAK TW: Regulation of expression of T cell gamma chain, L3T4 and Ly-2 messages in Abelson/Moloney virus-transformed T cell lines. *Eur J Immunol* 1988; **18:** 295.

SUTCLIFFE SB, HENKELMAN RM, POON PY: The potential application of magnetic resonance imaging (MRI) in radiation oncology. *In:* Withers HR, Peters LJ, eds. Innovations in Radiation Oncology. Berlin: Springer-Verlag, 1988: 201.

SUTCLIFFE SB, SIMPSON WJ, ROSEN IB: The place of external radiation therapy for differentiated and undifferentiated thyroid carcinoma. *Prog Surg* 1988; **19:** 147.

SUTHERLAND HJ, WALKER P, TILL JE: The development of a method for determining oncology patients' emotional distress using linear analogue scales. *Cancer Nursing* 1988; **11:** 303.

SUTHERLAND RM, RASEY JS, HILL RP: Tumor biology. *Am J Clin Oncol* 1988; **11:** 253.

SZUMOWSKI J, PLEWES DB: Fat suppression in the time domain in fast MR imaging. *Magn Reson Med* 1988; **8:** 345.

TAKIHARA Y, TKACHUK D, MICHALOPOULOS E, CHAMPAGNE E, REIMANN J, MINDEN M, MAK TW: Sequence and organziation of the diversity, joining, and constant region genes of the human T-cell delta-chain locus. *Proc Natl Acad Sci USA* 1988; **85:** 6097.

TANNOCK IF: Analysis of trials using chemotherapy for metastatic bladder cancer. *Prog Clin Biol Res* 1988; **260:** 487.

TANNOCK IF, BOYD NF, DeBOER G, ERLICHMAN C, FINE S, LAROCQUE G, MAYERS C, PERRAULT D, SUTHERLAND H: A randomized trial of two dose levels of cyclophosphamide, methotrexate, and fluorouracil chemotherapy for patients with metastatic breast cancer. J Clin Oncol 1988; **6:** 1377.

TANNOCK I, MOORE M: Quality assessment of clinical trials in bladder cancer. *Eur Urol* 1988; **14(Suppl 1):** 46.

TANNOCK IF, ROTIN D: Mechanisms of interaction between radiation and drugs with potential for improvements in therapy. *NCI Monogr* 1988; **6:** 77.

TANNOCK I, WARR D: Nonrandomized clinical trials of cancer chemotherapy: Phase II or III? J *Natl Cancer Inst* 1988; **80:** 800.

THIESSEN J, BASKERVILLE T, BUNTING P, ERLICHMAN C, KERR I, MOORE M, SOLDIN S: Cyclophosphamide, phosphoramide mustard, methotrexate, and 5-fluorouracil pharmacokinetics during repeated combination therapy. *Proc Am Assoc Cancer Res* 1988; **29:** A761. (Abstract)

TILL JE: Quality of survival. *In:* Withers HR, Peters LJ, eds. Innovations in Radiation Oncology. Berlin: Springer-Verlag, 1988: 25.

TIMOTHY AR, BREWIN T, CHAMBERLAIN J, HORWICH A, JENNETT B, KIND P, MAXWELL R, RAFTERY J, REES G, SELBY P, SKRANABEK P, SLEVIN ML, SMITH AJ, STOLL B, SUTCLIFFE S, TILL JE, WHITEHOUSE JMA: Cost versus benefit in non-surgical management of patients with cancer. *Br Med J* 1988; **297:** 471.

TKACHUK DC, GRIESSER H, TAKIHARA Y, CHAMPAGNE E, MINDEN M, FELLER AC, LENNERT K, MAK TW: Rearrangement of T-cell delta locus in lymphoproliferative disorders. *Blood* 1988; **72:** 353.

TRUEDEAU M, SHEPHERD FA, BLACKSTEIN ME, GOSPODAROWICZ M, FITZPATRICK P, MOFFATT KP: Intraocular lymphoma: Report of three cases and review of the literature. *Am J Clin Oncol* 1988; **11:** 126.

WANDL U, HOANG T, MINDEN M, MESSNER HA: Segregation of precursors with high proliferative potential from their differentiated progeny in a myeloma cell line. *J Cell Physiol* 1988; **136:** 384.

WANDTKE JC, PLEWES DB, McFAUL J: Improved pulmonary nodule detection with scanning equalization radiography: An ROC study. *Radiology* 1988; **169:** 23.

WANG C, KELLEHER CA, CHENG GY, MIYAUCHI J, WONG GG, CLARK SC, MINDEN MD, McCULLOCH EA: Expression of the CSF-1 gene in the blast cells of acute myeloblastic leukemia: Association with reduced growth capacity. *J Cell Physiol* 1988; **135:** 133.

WATANABE M, WATTS TH, GARIEPY J, HOZUMI N: Function and behavior of surface immunoglobulin receptors in antigen-specific T cell-B cell interaction. *Cell Immunol* 1988; **112:** 226.

WEINBERGER JM, BRIANT TD, CUMMINGS BJ, WONG CS: The role of surgery in the treatment of squamous cell carcinoma of the nasal vestibule. *J Otolaryngol* 1988; **17:** 372.

WONG CS, CUMMINGS BJ: The place of radiation therapy in the treatment of squamous cell carcinoma of the nasal vestibule: A review. *Acta Oncol* 1988; **27:** 203.

WOOD ML, RUNGE VM, HENKELMAN RM: Overcoming motion in abdominal MR imaging. *AJR* 1988; **150:** 513.

WOOD RE, HESSELING P, NORTJE CJ, MOUTON S: Pattern of jaw involvement in African Burkitt's lymphoma in the Cape Province and Nambia. *Dentomaxillofac Radiol* 1988; **17:** 57.

WOOD RE, HOUSEGO T, NORTJE CJ, PADAYACHEE A: Hemangiopericytoma of the mandible: Review of the literature and report of an intraosseous case. *Dentomaxillofac Radiol* 1988; **17:** 133.

WOODS G, LUND LA, NAIK M, LING V, OCHI A: Resistance of multidrug-resistant lines to natural killer-like cell-mediated cytotoxicity. *FASEB* J 1988; **2:** 2791.

WU GE, PAIGE CJ: VH gene family utilization is regulated by a locus outside of the VH region. *J Exp Med* 1988; **167:** 1499.

YAMASAKI K, SOLBERG LA Jr, JAMAL N, LOCKWOOD G, TRITCHLER D, CURTIS JE, MINDEN MM, MANN KG, MESSNER HA: Hemopoietic colony growth-promoting activities in the plasma of bone marrow transplant recipients. *J Clin Invest* 1988; **82:** 255.

YOUNG SD, MARSHALL RS, HILL RP: Hypoxia induces DNA overreplication and enhances metastatic potential of murine tumor cells. *Proc Natl Acad Sci USA* 1988; **85:** 9533.

ZUCKER PF, ARCHER MC: Alterations in pancreatic islet function produced by carcinogenic nitrosamines in the Syrian hamster. *Am J Pathol* 1988; **133:** 573.

ZUCKER PF, ARCHER MC: Steptozotocin toxicity to cultured pancreatic islets in the Syrian hamster. Cell Biol Toxicol 1988; **4:** 349.

OCTRF Toronto-Bayview Regional Cancer Centre:

ANDERSON JE, WILLAN AR: Estimating the size of family practice population: Quadratic odds estimation. *Med Care* 1988; **26:** 1228.

BELCH A, SHELLEY W, BERGSAGEL D et al: A randomized trial of maintenance versus no maintenance melphalan and prednisone in responding multiple myeloma patients. *Br J Cancer* 1988; **57:** 94.

BERINSTEIN N, LEVY S, LEVY R: Expression of a silent allele creates idiotype diversity in a human B lymphoma cell line. *FASEB* J 1988; **2:** 4. (Abstract 872)

BERINSTEIN N, STARNES C, LEVY R: Specific enhancement of the therapeutic effect of anti-idiotype antibodies on a murine B cell lymphoma by IL-2. *J Immunol* 1988; **140:** 2839.

BERINSTEIN N, STARNES C, BASHAM T, LEVY R: Specific enhancement of the therapeutic effect of anti-idiotype antibodies by IL2 in the treatment of a murine B cell lymphoma. *Proc Am Assoc Cancer Res* 1988; **29:** 417. (Abstract 1661)

BERINSTEIN N, STARNES C, LEVY R: Specific enhancement of the therapeutic effect of anti-idiotype antibodies on a murine B cell lymphoma by IL-2. *J Immunol* 1988; **140:** 2839.

BURNS BF, COMRIE W, WILLAN AR, McCAUGHEY E: Observer variation in the pathological diagnosis of malignant lymphoma in Canada. *Cancer* 1988; **62:** 314.

CAREY MS, DEMBO AJ, PELOQUIN A: Facteurs histologiques de pronostic des tumeurs epitheliales de l'ovaire. *In:* Cappelere P, ed. Progres en Gynecologie: Tumeurs de L'Ovaire. Paris: Doin, d'Quenlen, 1988: 27.

CRUESS AF, WILLAN AR et al: Argon (green) versus krypton (red) laser photocoagulation of subretinal neovascularization. *Retinal Dis* 1988; **2:** 19.

CRUESS AF, WILLIAMS JC, WILLAN AR: Argon green and krypton red laser treatment of diabetic macular edema. *Can J Ophthalmol* 1988; **23:** 262.

DEITEL M, STONE E, HASSANALI AK, WILK E, SUTHERLAND DJA: Gynecologic-obstetric changes after loss of massive excess weight following bariatric surgery. *J Am Col Nutr* 1988; **7:** 147.

DEMBO AJ: Hyperfractionation of whole-abdomen radiation therapy: Salvage treatment of persistent ovarian carcinoma following chemotherapy. *Gynecol Oncol* 1988; **31:** 135.

FERRIS FD, KERR IG, De ANGELIS C, SONE M: Inpatient narcotic infusion experience. *J Palliat Care* 1988; **4:** 75.

FYLES AW, DEMBO AJ: Radioterapia del carcinoma epitelial de ovaro. *Revisiones en Cancer Ediciones, SA (Madrid)* 1988; **2:** 28.

ISCOE N, McKEE J, ARENSON AM, SZALAI J: Observer error in the interpretation of hepatic ultrasound in patients with neoplastic liver disease. *J Clin Ultrasound* 1988; **16:** 577.

JENKIN D, DOYLE J: Paediatric Hodgkin's disease: Late results and toxicity. *Br J Radiol* 1988; **Suppl 22:** 65. (Abstract 36)

JENKIN RDT, DOYLE J: Pediatric Hodgkin's disease: Later results and toxicity – the Toronto experience. *In:* Kamps WA, ed. Hodgkin's Disease in Children. Boston: Kluwer Academic Publishers, 1988: 247.

KELLEN JA, SUTHERLAND DJA: Tamoxifen tolerance and steroid receptors in a tumor model. *In Vivo* 1988; **2:** 299

KERR IG, SONE M, De ANGELIS C, ISCOE N, MacKENZIE R, SCHUELLER T: Continuous narcotic infusion with patient-controlled analgesia for chronic cancer pain in outpatients. *Ann Intern Med* 1988; **65:** 10.

KLAASSEN D, SHELLEY W, STARREVELD A, et al: Early stage ovarian cancer: A randomized clinical trial comparing whole abdominal radiotherapy, melphalan and intraperitoneal chromic phosphate. *J Clin Oncol* 1988; **6:** 1254.

MICHAELS HB: Electromagnetic fields: Carcinogenic or not? *Engin Dimens* 1988; **9:** 6. (Letter to the Editor)

PRITCHARD KI: The role of tamoxifen in the treatment and prevention of breast cancer: The article reviewed (Editorial). *Oncology* 1988; **2:** 25.

PRITCHARD KI, MEMBERS OF WRITING COMMITTE: The effects of adjuvant tamoxifen and of cytotoxic therapy on mortality in early breast cancer: An overview of 61 randomized trials among 28,896 women. *N Engl J Med* 1988; **319:** 1681.

PRITCHARD KI, ELHAKIM T, DeBOER G, TORRANCE GW, GOODWIN PJ, CLARK RM: An economic analysis of the use of postoperative breast irradiation following partial mastectomy and axillary node dissection in axillary node negative breast cancer. *Clin Invest Med* 1988; **11:** C95.

PRITCHARD KI, ELHAKIM T, DeBOER G, TORRANCE GW, GOODWIN PJ, CLARK RM: An economic analysis of the use of postoperative breast irradiation following partial mastectomy and axillary node dissection in axillary node negative breast cancer. *Proc Am Soc Clin Oncol* 1988; **7:** 13.

RICHART R, THOMAS G, BORONOW R, MONAGHAN J, HACHNER NF: Microscopic vulvar carcinoma: A new concept symposium. *Contemp Ob Gyn* 1988; **32:** 117.

RYAN CA, WHERRETT BA, WILLAN AR: Home nebulizers in childhood asthma: Parents perceptions and practices. *Clin Pediatr* 1988; **27:** 420.

SHAW P, BUCKMAN R, LAW J, BAUMAL R, MARKS A: Reactivity of tumour cells in malignant effusions with a panel of monoclonal and polyclonal antibodies. *Tumour Biol* 1988; **9:** 101.

SIWEK RA, KODAMA R, SRIGLEY J, KLOTZ L: Tissue effects of neo-dymium-YAG laser irradiation of pig ureter. *Phys Med Biol* 1988; **33(Suppl 1):** 18.

WILLAN AR: Using the maximum test statistic in the two period crossover clinical trial. *Biometrics* 1988; **44:** 211.

WILLAN AR, MacKENZIE TA: The severity of illness and laboratory testing. *Can J Publ Health* 1988; **79:** 435.

WODINSKY HB: Canadian cancer centres. *In:* Nathanson S, Lerman D, eds. Outpatient Cancer Centres: Implementation and Management. Chicago: The American Hospital Association Press, 1988: 233.

WODINSKY HB: Finding your way: Alternative models for palliative care funding in Canada. *Pain Management Newsletter* 1988; **1:** 1.

WODINSKY HB: Outpatient versus inpatient palliative pain control: Update to a preliminary cost comparison. *J Palliat Care* 1988; **4:** 3.

WODINSKY HB EGAN D, MARKEL F: Product line management in oncology: Canadian Perspectives. *Health Hosp Serv Admin* 1988; **33:** 221.

WODINSKY HB, SONE M, KERR IG: Outpatient palliative pain control. *Dimens Health Serv* 1988; **65:** 10.

OCTRF Head Office:

BOICE JD, KREIGER N, ENGHOLM G et al: Radiation dose and second cancer risk in patients treated for cancer of the cervix. *Radiat Res* 1988; **116:** 3.

KREIGER N: Osteoporosis in an aging population. *Chron Dis Can* 1988; **9:** 85.

ROBLES SC, MARRETT LD, CLARKE EA, RISCH HA: An application of capture-recapture methods to the estimation of completeness of cancer registration. *J Clin Epidemiol* 1988; **41:** 495.

WALTER SD, MARRETT LD, MISHKEL NR: Effect of cover letter on control response rates in cancer studies. *Am J Epidemiol* 1988; **127:** 691.

University of Toronto:

De HARVEN EP, HE S, BOOTSMA G, CONNOLLY JG: Phenotypic heterogeneity of blood group antigens partially deleted from the transformed bladder urothelium. *J Urol* 1988; **169:** 368A.

LEA PJ, PAWLOWSKI A, PERSAD SD, MENON IA, HABERMAN HF: Ultrastructural carcinoma cells by ultraviolet-visible radiation in the presence of melanins. *Pigment Cel Res* 1988; **1:** 402.

MOBBS BG, JOHNSON IE: Basal and estrogen-stimulated hormone receptor profiles in four R3327 rat prostatic carcinoma sublines in relation to histopathology and androgen sensitivity. *Cancer Res* 1988; **48:** 3077.

MOBBS BG, JOHNSON IE: The effect of estrogen on the hormone receptor profiles of four Dunning tumor sublines with differing histopathology and androgen sensitivity. *Proc Am Assoc Cancer Res* 1988; **29:** 241. (Abstract 956)

WINDSOR

OCTRF Windsor Regional Cancer Centre:

DECKER D, KINZIE J, EVANS R, ABU-ZAHRA H, AL-SARRAF M: Pilot study of combination 5-fluorouracil, cisdiamminedichloroplatinum II, and radiation therapy for grade III and IV astrocytomas. *Am J Clin Oncol* 1987; **10:** 444.